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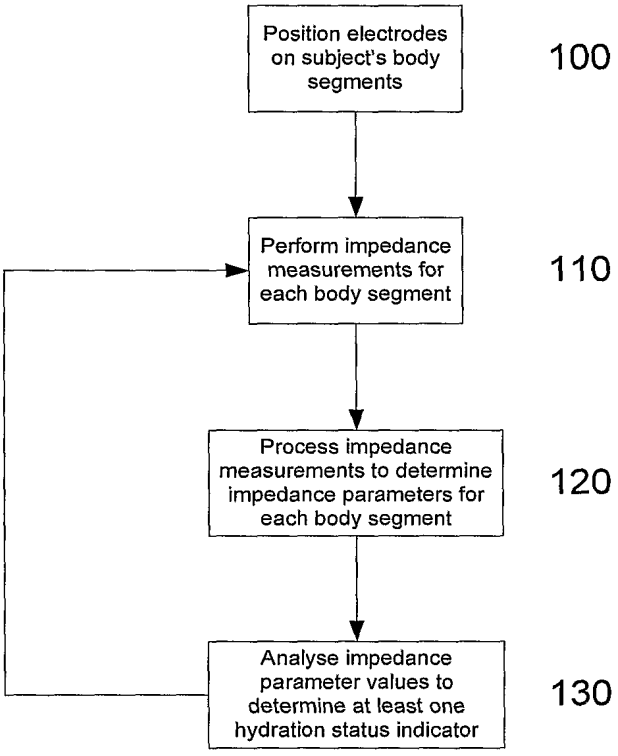

(57) Abstract: A method of determining an indication of the hydration status relating to a subject. The method includes determining a measured impedance value for at least one body segment, and then; for each body segment, using the measured impedance values to determine at least one indicator at least partially indicative of a level of extracellular fluid. Indicators can then be used to determine an indication of the hydration status.

WO 2007/041783 A1

HYDRATION STATUS MONITORING

Background of the Invention

The present invention relates to a method and apparatus for determining one or more indicators of a subject's hydration status and in particular to a method and apparatus for monitoring a subject's hydration status during a dialysis procedure.

Description of the Prior Art

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that the prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

One existing technique for determining biological parameters relating to a subject, involves the use of bioelectrical impedance. This involves measuring the electrical impedance of a subject's body using a series of electrodes placed on the skin surface. Changes in electrical impedance at the body's surface are used to determine parameters, such as changes in fluid levels, associated with the cardiac cycle or oedema.

Maintaining hemostasis during hemodialysis is recommended to minimise cardiovascular and other associated risks. Oedema is difficult to detect until the interstitial fluid volume has risen to approximately 30% above normal, whilst severe dehydration can develop before the onset of clinical symptoms. The current method of evaluating hydration status of dialysis patients based on blood pressure and body weight changes over time can be misleading since these parameters are complex variables related to other physiologic mechanisms.

Summary of the Present Invention

In a first broad form the present invention provides a method of determining an indication of the hydration status relating to a subject, the method including, in a processing system:

a) determining a measured impedance value for at least one body segment;
b) for each body segment, and using the measured impedance values, determining at least one indicator, the indicator being at least partially indicative of a level of extracellular fluid;
c) determining an indication of the hydration status using at least one determined indicator.

Typically the method includes, in the processing system:

a) comparing the at least one indicator to at least one of:

i) a predetermined reference;

ii) an indicator determined for at least one other body segment; and,

iii) a previously determined indicator; and,

b) determining an indication of the hydration status using the results of the comparison.

Typically the reference includes at least one of:

a) a predetermined threshold;

b) a tolerance determined from a normal population;

c) a predetermined range; and,

d) an indicator previously determined for the subject.

Typically the indicator is at least one of:

a) an index (*I*)of the ratio of extra- to intra-cellular fluid; and,

b) an extracellular fluid volume.

Typically the method includes, in the processing system:

a) determining a plurality of measured impedance values for each body segment, each measured impedance value being measured at a corresponding measurement frequency; and,

b) determining impedance parameter values based on the plurality of measured impedance values, the indicator being at least partially based on the determined impedance parameter values.

Typically the parameter values include R_0 and R_∞, wherein:

R_0 is the resistance at zero frequency; and,

R_∞ is the resistance at infinite frequency.

Typically the method includes:

a) monitoring changes over time for at least one of:

i) R_0;

ii) R_∞;

iii) a difference between R_0 and R_∞;

b) a vector indication of an impedance measurement.

Typically the method includes, in the processing system:

a) determining values for parameters R_0 and R_∞ from the measured impedance values; and,

b) determining the indicator by calculating the index (*I*) using the equation:

$$I = \frac{R_\infty}{R_0 - R_\infty}$$

Typically the method includes, in the processing system, determining the parameter values using the equation:

$$Z = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega\tau)^{(1-\alpha)}}$$

where:

Z is the measured impedance at angular frequency ω,

τ is a time constant, and

α has a value between 0 and 1.

Typically the method includes, in the processing system:

a) determining the impedance of each body segment at four discrete frequencies; and,

b) determining values for the parameters by solving the equation using four simultaneous equations.

Typically the method includes, in the processing system, determining the parameter values by:

a) determining a complex impedance locus using the measured impedance values; and,

b) using the complex impedance locus to determine the parameter values.

Typically the indicator for a body segment is the extracellular fluid volume determined using the equation:

$$ECV_{Segment} = C_{Segment}\rho_{Segment}\left(\frac{L^2_{Segment}}{R_{Segment}}\right)$$

Where ECV = Extracellular fluid volume

$C_{Segement}$ = Geometry Constant which is 1 for an arm or leg and 4 for the thoracic cavity

$L_{Segment}$ = Length of the segment in cm

$R_{Segment}$ = Resistance of the segment in Ohm

$\rho_{Segment}$ = Resistivity coefficient which is nominally 47 Ohm/ cm

Typically the method includes determining an indicator for the entire body the equation:

$$ECV_{Total} = 2(ECV_{arm} + ECV_{leg}) + ECV_{trunk}$$

Typically the second body segment and the at least one other body segment are different types of body segment.

Typically the body segments are limbs.

Typically the body segment includes at least one of:

a) a calf; and,

b) a bicep.

Typically the method includes, in the computer system:

a) determining a correction factor; and

b) determining the hydration status using the correction factor.

Typically the correction factor is indicative of at least one of:

a) a subject orientation or posture;

b) a subject skin temperature; and,

c) a subject ethnicity.

Typically the method includes, in the computer system:

a) determining a subject orientation; and

b) determining the hydration status using the orientation.

Typically the method includes, in the computer system:

a) determining a first indicator at a first subject orientation;

b) determining a second indicator at a second subject orientation; and

c) determining the hydration status using the difference between the first and second indicators.

Typically the method includes, in the computer system:

a) determining a first indicator at a first time;

b) determining a second indicator at a second time; and

c) determining the hydration status using the difference between the first and second indicators.

Typically the method includes, in the computer system, displaying an indication of at least one of:

a) parameter values;

b) the indicator;

c) an extracellular fluid volume; and,

d) a ratio of extra-cellular to intra-cellular fluid.

Typically the method includes, in the processing system:

a) receiving data representing at least one measured impedance value; and,

b) generating a representation of the at least one measured impedance value.

Typically the method includes, in the processing system:

a) selecting a representation type based on a selected impedance measurement type; and,

b) generating the representation in accordance with the selected representation type.

Typically the representation is in the form of at least one of:

a) a Complex impedance plot;

b) an argand diagram;

c) a list of impedance values;

d) a reactance against frequency plot; and,

e) resistance against frequency plot.

Typically the method includes, in the processing system:

a) receiving data representing at least one measured impedance value;

b) processing the at least one measured impedance value to determine at least one impedance parameter; and,

c) generating a representation of the at least one impedance parameter.

Typically the method includes, in the processing system:

a) causing one or more electrical signals to be applied to the subject using a first set of electrodes, the one or more electrical signals having a plurality of frequencies;

b) determining an indication of electrical signals measured across a second set of electrodes applied to the subject in response to the applied one or more signals;

c) determining from the indication and the one or more applied signals, an instantaneous impedance value at each of the plurality of frequencies; and,

d) determining the indicator using the instantaneous impedance values.

Typically the electrodes are positioned in accordance with the theory of equal potentials.

Typically the positioning of the electrodes includes:

a) a first current supply electrode positioned on a limb being measured;

b) a second current supply electrode on a second limb on a the same lateral side of the subject as the limb being measured;

c) a first voltage electrode positioned on a limb being measured; and,

d) a second voltage electrode positioned on a third limb contra-lateral to the limb being measured.

Typically the processing system is coupled to a measuring device, and wherein the method includes, in the processing system:

a) generating instructions; and,

b) transferring the instructions to the measuring device, the measuring device being responsive to the instructions to cause the impedance measurements to be performed.

Typically the processing system forms part of a measuring device.

Typically the measuring device includes at least two channels, each channel being adapted to measure the impedance across a respective body segment, and wherein the method includes, in the processing system, causing at least one impedance measurement to be performed using each channel.

Typically the measuring device includes a processor, and wherein the processor is for:

a) receiving the instructions; and,

b) causing one or more impedance measurements to be performed using the instructions.

In a second broad form the present invention provides apparatus for detecting tissue oedema in a subject, the apparatus including a processing system for:

a) determining a measured impedance value for at least one body segment;

b) for each body segment, and using the measured impedance values, determining at least one indicator, the indicator being at least partially indicative of a level of extracellular fluid;

c) determining an indication of the hydration status using at least one determined indicator.

Typically the apparatus includes:

a) a current supply for generating an alternating current at each of a plurality of frequencies;

b) at least two supply electrodes for applying the generated alternating current to a subject;

c) at least two measurement electrodes for detecting a voltage across the subject; and,

d) a sensor coupled to the measurement electrodes for determining the voltage, the sensor being coupled to the processing system to thereby allow the processing system to determine the measured impedances.

Typically the apparatus is adapted to perform the method of the first broad form of the invention.

In a third broad form the present invention provides a method for use in dialysis of a subject, the method including, in a processing system:

a) determining one or more impedance values for at least one body segment;

b) for each body segment, and using the measured impedance values, determining at least one indicator; and,

c) selectively controlling the dialysis the subject using at least one determined indicator.

It will be appreciated that the broad forms of the invention may be used individually or in combination, and may be used in performing or controlling dialysis in subjects such as humans.

Brief Description of the Drawings

An example of the present invention will now be described with reference to the accompanying drawings, in which: -

Figure 1 is a schematic of an example of impedance determination apparatus;

Figure 2 is a flowchart of an example of an outline of a process for determining indicators of hydration status;

Figures 3A and 3B are a flow chart of an example of a detailed process for determining indicators of hydration status;

Figures 4A and 4B are examples of a GUI used in providing subject details;

Figure 5A is an example of a GUI used in providing electrodes on a subject;

Figures 5B and 5C are examples of typical electrode placements;

Figures 5D is an example of an electrode configuration used in measuring the impedance of a subject's right arm;

Figure 5E is an example of a GUI used in performing impedance measurements;

Figures 6A to 6D are examples of a GUI used in viewing measured impedance parameters;

Figures 7A and 7B are examples of a GUI used in selecting references;

Figures 7C to 7I are examples of a GUI used in presenting the results of an impedance analysis;

Figure 8 is an example of a GUI used in performing total body impedance measurements;

Figure 9 is a schematic of a second example of impedance determination apparatus; and,

Figure 10 is a schematic of a GUI used in configuring the apparatus of Figure 9.

Detailed Description of the Preferred Embodiments

An example of apparatus suitable for performing an analysis of a subject's impedance will now be described with reference to Figure 1.

As shown the apparatus includes a monitoring device 1 including a processing system 10 having a processor 20, a memory 21, an input/output (I/O) device 22, and an optional external interface 23,

coupled together via a bus 24. The external interface can be used to couple the measuring device 1 to one or more peripheral devices 4, such as an external database or computer system, barcode scanner, dialysis machine, any other required sensors, or the like. The processing system 10 is coupled to a signal generator 11 and a sensor 12, via a processing module 17, as shown.

In use the signal generator 11 and the sensor 12 are selectively coupled to respective electrodes 13A, 13B, 13C, 13D, 15A, 15B, 15C, 15D provided on a subject S, via a multiplexer 18, and connecting leads L, as shown.

The processing system 10 and processing module 17 are adapted to generate control signals, which cause the signal generator 11 to generate one or more alternating signals, such as voltage or current signals. These signals are then transferred to a selected pair of electrodes 13A, 13B, 13C, 13D by the multiplexer 18, allowing the alternating signals to be applied across a respective segment of the subject S, depending on the position of the selected pair of electrodes 13A, 13B, 13C, 13D. The sensor 12 is then connected to selected ones of the electrodes 15A, 15B, 15C, 15D, using the multiplexer 18, allowing the voltage across or current through the respective segment of the subject S to be measured. The processing system and processing module 17 are adapted to generate control signals to control the switching of multiplexer 18.

The sensor 12 transfers appropriate signals to the processing system 10, allowing the impedance of the respective segment of the subject S to be determined, as will be described in more detail below.

In any event, by using the multiplexer to selectively connect different pairs of the electrodes 13A, 13B, 13C, 13D to the signal generator 11, and pairs of the electrodes 15A, 15B, 15C, 15D to the sensor 12, this allows the impedance across different segments of the subject S to be measured. In general, the use of a particular combination of electrodes for measuring a particular body segment is referred to as a channel, and accordingly, it will be appreciated that the above described apparatus provides multi-channel functionality, allowing different body segments to be measured through appropriate switching of the multiplexer. However, multi-channel functionality may be achieved using other configurations, such as by providing a respective processing module 17, signal generator 11 and sensor 12 for each channel.

In any event, the processing system 10 may be any form of processing system which is suitable for generating appropriate control signals and interpreting voltage data to thereby determine the subject's bioelectrical impedance, and optionally the subject's dry mass to aid in dialysis.

The processing system 10 may therefore be a suitably programmed computer system, such as a laptop, desktop, PDA, smart phone or the like. Alternatively the processing system 10 may be formed from specialised hardware. Similarly, the I/O device may be of any suitable form such as a touch screen, a keypad and display, or the like.

Similarly, the processing module 17 is adapted to perform specific processing tasks, to thereby reduce processing requirements on the processing system 10. Accordingly, the processing module may be custom hardware, or the like, and in one example is formed from a Field Programmable Gate Array (FPGA), although any suitable processing module, such as a magnetologic module, may be used.

It will be appreciated that the processing system 10, the processing module 17, the signal generator 11, the sensor 12 and the multiplexer 18 may be integrated into a common housing and therefore form an integrated device. Alternatively, the processing system 10 may be connected to the signal generator 11 and the sensor 12 via wired or wireless connections. This allows the processing system 10 to be provided remotely to the signal generator 11 and the sensor 12. Thus, the signal generator 11 and the sensor 12 may be provided in a unit near, or worn by the subject S, whilst the processing system is situated remotely to the subject S.

Once the electrodes 13A, 13B, 13C, 13D are positioned, an alternating signal is applied to the subject S using a selected pair of the electrodes 13A, 13B, 13C, 13D. This may be performed either by applying an alternating signal at a plurality of frequencies simultaneously, or by applying a number of alternating signals at different frequencies sequentially. However the frequency range of the applied signals will also depend on the analysis being performed.

In the preferred implementation the applied signal is a frequency rich current from a current or voltage source, clamped or limited, so it does not exceed the maximum allowable subject auxiliary current. The signal can either be an impulse function or a voltage signal where the current is measured so it does not exceed the maximum allowable subject auxiliary current.

A potential difference and/or current is measured between a pair of the electrodes 15A, 15B, 15C, 15D.

To ensure accurate measurement of the impedance, buffer circuits are placed in connectors that are used to connect the voltage sensing electrodes 15 to the leads L. This ensures accurate sensing of the voltage response of the subject S, and in particular helps eliminate contributions to the measured voltage due to the response of the leads L.

This in turn greatly reduces artefacts caused by movement of the leads L, which is particularly important during dialysis as sessions are usually last for several hours and the subject will move around and change seating positions during this time.

A further advantage of this configuration is that the voltage is measured differentially, meaning that the sensor used to measure the potential at each electrode 15 only needs to measure half of the potential as compared to a single ended system. This in turn reduces the potential across the multiplexer 18, thereby greatly reducing capacitive leakage in the multiplexer, resulting in a corresponding increase in accuracy.

The current measurement system may also have buffers placed in the connectors between the electrodes 13 and the leads L. In this instance, current is also driven or sourced through the subject S symmetrically, which again greatly reduced the parasitic capacitances by halving the common-mode current. Another particular advantage of using a symmetrical system is that the micro-electronics built into the connectors for each electrode 13 also reduces parasitic capacitances that arise when the subject S, and hence the leads L move.

In any event, the acquired signal and the measured signal will be a superposition of potentials generated by the human body, such as the ECG, and potentials generated by the applied current.

Optionally the distance between the inner pair of electrodes 15A, 15B, 15C, 15D may be measured and recorded. Similarly, other parameters relating to the subject may be recorded, such as the height, weight, age, sex, health status, any interventions and the date and time on which they occurred and other information, such as current medication, may also be recorded.

The acquired signal is demodulated to obtain the impedance of the system at the applied frequencies.

One suitable method for demodulation of superposed frequencies is to use a Fast Fourier Transform (FFT) algorithm to transform the time domain data to the frequency domain. This is typically used when the applied current signal is a superposition of applied frequencies. Another technique not requiring windowing of the measured signal is a sliding window FFT.

In the event that the applied current signals are formed from a sweep of different frequencies, then it is more typical to use a processing technique such as multiplying the measured signal with a reference sine wave and cosine wave derived from the signal generator and integrating over a whole number of cycles. This process totally rejects any harmonic responses and significantly reduces random noise.

Other suitable digital and analog demodulation techniques will be known to persons skilled in the field.

Impedance or admittance measurements are determined from the signals at each frequency by comparing the recorded voltage and current signal. The demodulation algorithm will produce an amplitude and phase signal at each frequency.

An example of the process of performing impedance measurements and determining indicators of hydration status utilising the apparatus to Figure 1 will now be described with reference to Figure 2.

At step 100 an operator of the apparatus positions electrodes 13, 15 on the subject before connecting leads to the electrodes 13, 15 so as to allow the apparatus to measure the impedance of a number of different body segments independently.

This will typically involve having the operator place a number of electrodes 13, 15 on the subject S and then connecting leads between the electrodes 13, 15 and the multiplexer 18 to allow the measuring device 1 to determine the impedance of respective body segments by selectively making measurements via the various channels.

At step 110 the measuring device 1 will operate to perform impedance measurements by generating an appropriate current sequence and applying this to the subject S via a pair of the electrodes 13A, 13B, 13C, 13D. This is typically performed in sequence for each channel, thereby allowing measurements to be determined for each body segment in turn.

At step 120 the measuring device 1 operates to process the impedance measurements so as to determine impedance parameters for each body segment, which can then in turn be analysed to determine indicators of the subject's current hydration status.

This process will now be described in more detail with respect to Figures 3A and 3B, and with reference to the graphical user interface (GUI) screen shots shown in Figures 4, 5, 6 and 7.

In the example set out in Figure 3A at step 400 the operator selects that hydration status monitoring is to be performed. This may be required for example in the event that the measuring device 1 is able to perform a number of different types of measurement procedure, and typically involves having an operator select hydration status monitoring from a list of available measurement types. The available measurement types are typically determined by the processing system 10 either from the memory 21, or alternatively downloaded via the external interface 23 and are based on predetermined profiles

which provide suitable instructions to allow the measuring device 1 to perform the required impedance measurements.

At this stage, the processing system 10 may download appropriate firmware into the FPGA 17, allowing the correct impedance measurement process to be performed by the FPGA.

At step 410 the measuring device 1 displays a GUI 1000 as shown in Figure 4A. The GUI includes a number of fields, shown generally at 1001, which allow data regarding the individual to be provided. The data includes information such as name, address, sex, height, weight, limb length or the like. Additionally, an indication of limbs at risk from oedema can be input as shown at 1002, as this can be used in assisting with the analysis.

This is used to create a subject record, which is typically stored in a subject database accessed via the external interface 23, or the like. The subject record includes the subject data, and details of any performed impedance measurements for the respective subject, thereby allowing the subject record to form a subject history for use in longitudinal analysis. Thus, it will be appreciated that in the event that a record already exists for the current subject, then the operator can perform a search to retrieve the record from the database. The database is typically a HL7 compliant remote or local database.

In one example, the subject can be provided with a wristband or the like which includes coded data indicative of the subject identifier. In this case, the measuring device 1 can be coupled to a peripheral device 4 for determining the subject identifier. Thus, for example, the data may be in the form of a barcode, with the peripheral device 4 being a barcode scanner. It will be appreciated however that any suitable mechanism could be used for encoding the subject identifier such as RFID (Radio Frequency ID) tags could be used, in which case the peripheral device will be a corresponding reader.

In this example, the barcode reader detects the barcode provided on the subject's wrist band, and determines a subject identifier from the detected barcode. The barcode reader provides data indicative of the sensed subject identifier to the processing system 10, thereby allowing the processing system 10 to access the subject record from the database.

Alternatively however the subject identifier could be entered manually by an operator, for example, by using the I/O device 22.

In the event that information such as limb length is not available then the measuring device 1 can estimate these from other subject data, such as a the subject height, using anthropometric tables, or the like. These can be customised by the operator of the measuring device, or can be downloaded from a central repository such as the database.

In any event, once this information is provided or otherwise determined, the processing system will update the GUI 1000 as shown in Figure 4B to display any previously measured impedance values, which may be used as reference data, as will be described in more detail below. Searching, editing and creation of records using the input controls shown generally at 1004.

At step 430 the processing system 10 generates a GUI 1010, an example of which is shown in Figure 5A, and which is used in allowing the operator to provide electrode connections. In this example, the GUI 1010 includes an indication of subject details at 1011. A representation 1012 of the subject is provided, which shows general electrode connection points 1013, 1015, indicating where on the subject electrodes 13, 15 should be provided.

The general arrangement is to provide electrodes on the hand at the base of the knuckles and between the bony protuberances of the wrist, as shown in Figure 5B, and on the feet at the base of the toes and at the front of the ankle, as shown in Figure 5C.

It will be appreciated that this configuration uses the theory of equal potentials, allowing the electrode positions to provide reproducible results for impedance measurements. For example, when one of the channels is being used to measure the impedance of the right arm, the electrode configuration used is as shown in Figure 5D.

In this configuration, current is injected between electrodes 13A and 13C, with the electrodes 15A positioned as shown, and the electrode 15B being placed anywhere along the left arm, since the whole arm is at an equal potential. This is advantageous as it greatly reduces the variations in measurements caused by poor placement of the electrodes by the operator. It also greatly reduces the number of electrodes required to perform segmental body measurements, as well as allowing the limited connections shown to be used to measure each of limbs separately.

In one example, the current electrodes are provided on one hand and one foot, whilst the voltage electrodes are positioned a set distance apart on a calf or on a bicep. This is particularly advantageous as fluid levels in the calf are generally sensitive to changes in the subject's posture, whilst fluid levels in the bicep are relatively posturally invariant. Consequently, comparison of impedance measurements made at a subject's calf and bicep can be useful in detecting the subject's optimal fluid state, whilst taking into account changes in posture, as will be described in more detail below.

The GUI 1010 also displays details for each limb at 1017A, 1017B, 1017C, 1017D, including an indication of whether the limb is an at risk limb, which is a limb suffering from vascular insufficiency, as caused for example by surgery, obesity, an accident, or the like. An example of

acquired vascular insufficiency is lymphoedema. This is also shown on the representation 1012 at 1017E.

An instruction field is shown generally at 1018 and this is provided to display instructions to the operator, with an indication of the selected measurement procedure being shown at 1019, and general measuring device status information being provided at 1020. A comments field 1021 can also be used to record comments regarding the measurements made.

At this stage the operator typically updates the weight of the subject in the subject details 1011, which may undergo significant variations over time due to changes in fluid levels within the subject's body. The operator may also re-specify the at risk limbs, which is useful when a subject develops further vascular insufficiency in a limb. For example, a subject may start off with unilateral vascular insufficiency of the left leg and over time may develop a vascular insufficiency in the right leg. This leg can be recorded at that point as being affected by the use of the "at risk" check boxes.

Once the weight and comments are entered the measurement procedure can be initiated by clicking the "ok button" 1022. At this stage, both the weight and comments for each measurement are recorded as part of the corresponding subject record in the subject database. This allows the practitioner to track weight and clinical comments over the period of measurement as well as between different measurement periods.

Thus, it will be appreciated from the following that the process can be used to measure the dry mass of the subject, not only during a dialysis session, but also between different dialysis sessions, thereby further enhancing the ability of the system to determine any deviation from optimal haemostasis conditions. The system can also be used to track additional information, relating to details of potential triggers, such as the subject's food and drink consumption. This coupled with the fact that the system can accurately determine indicators of dry mass and hydration status can be used with trigger information to assess which potential triggers have a material, and adverse effect on the subject and the dialysis process. This in turn allows the triggers to be avoided in future.

At step 440, the measuring device 1 optionally checks electrode continuity. This can be achieved based on the theory of equipotentials by comparing potentials measured at different ones of the electrodes. In particular, the process can measure the potential at different electrodes on a given limb, and these should be identical in accordance with the equipotential theory. In the event that the measured potentials are different, this indicates that there is a fault, such as a problem with the connection to one of the electrodes.

Additionally, or alternatively, it is possible to examine raw data from the applied current signal and the differential voltage signal, as acquired from the signal generator 11 and the sensor 12, and examine either the absolute magnitude of the signals, or a signal to noise ratio. In this instance, if either the absolute magnitude of the voltage signal, or the signal to noise ratio, are below respective thresholds, then this indicates a problem with the electrode connections.

Any problem with the electrode connections can be indicated to the operator of the measuring device 1 allowing the connection problem to be corrected.

If the electrode continuity is checked and it is determined the electrodes are not configured or working correctly, the process returns to step 430 so that the operator replaces or repositions the electrodes.

Otherwise, at step 450, the measuring device 1 optionally measures ECG signals. This can be achieved either through the use of a 5 lead ECG measurement process that utilises the same electrodes as used in measuring the impedance. Alternatively, optional additional leads may be used to allow for recording full 12 lead ECG measurements. If ECG signals are measured, these can be used to monitor an R-R interval trend using chaotic predictors. This can be used to determine a warning of the onset of a malignant or unstable arrhythmia, up to 10 minutes prior to the arrhythmia developing.

Additionally, this can be used to monitor cardiac output allowing a warning to be sounded when cardiac output starts to drop during dialysis. This may indicate that the patient will not have adequate cardiac function if more fluid is removed. This can be used to determine the optimum fluid loading for a patient suffering from cardiac disease who also requires dialysis.

At step 460, the measuring device 1 optionally measures and trends blood pressure signals.

At step 470, the measuring device 1 then performs the required impedance measurements, with general measuring device status information being provided at 1020. To achieve this, the monitoring device 1 applies the required current signals to one of the body segments, via a respective one of the channels A, B, measuring the resulting current and voltage across the body segment. This allows instantaneous impedance values to be determined at a number of different frequencies f_i, for the respective body segment, which are then stored at step 480.

The measuring device 1 repeats this for each of the measurement channels, so that impedance measurements are determined for each of the body segments separately.

At step 490 the measuring device 1 operates to determine impedance parameters for each body segment. Typically this includes parameters such as the impedance at zero, characteristic and infinite frequencies (R_0, Z_c, R_∞). These can be derived based on the impedance response of the subject, which at a first level can be modelled using the equation (1):

$$Z = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega\tau)} \qquad (1)$$

where: R_∞= impedance at infinite applied frequency,
R_0= impedance at zero applied frequency,
ω = angular frequency,
τ is the time constant of a capacitive circuit modelling the subject response.

However, the above represents an idealised situation which does not take into account the fact that the biological tissues are an imperfect system. Taking this into account leads to a modified model, called the Cole model, in which:

$$Z = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega\tau)^{(1-\alpha)}} \qquad (2)$$

where α has a value between 0 and 1 and can be thought of as an indicator of the deviation of a real system from the ideal model.

The value of the impedance parameters R_0 and R_∞ may be determined in any one of a number of manners such as by:

- solving simultaneous equations based on the impedance values determined at different frequencies;
- using iterative mathematical techniques;
- extrapolation from a "Complex impedance plot" (also sometimes referred to as a "Wessel" or "Cole-Cole" plot) or argand diagram;
- performing a function fitting technique, such as the use of a polynomial function.

At this stage the processing system 10 can also be adapted to test adherence of the measurements to the Cole model. In particular, the Cole model assumes that the impedance measurements lie on a semi-circular impedance locus. Accordingly, the processing system 10 can determine if the measured values fit a semi-circular locus to thereby determine if the Cole model is satisfied. Alternatively, the

measured impedance parameter values can be compared to theoretical values derived using the equation (2), to thereby allow the degree of concordance to the Cole model to be determined.

In the event that the Cole model is not satisfied, an indication of this can be provided to the operator allowing an appropriate analysis technique to be utilised.

Once the parameters have been determined, these can optionally be viewed using a GUI, an example of which is shown in Figures 6A to 6D. In this example, the GUI 1030 includes subject details at 1031, and a measurement selection inputs 1032. This allows the operator to select measurements of interest, which in this example includes measurements from the left arm. Once the measurements are selected, the processing system 10 displays an overview of parameters determined from the impedance measurements at 1033.

A number of tabs 1034 can then be used to allow different representations of the measured impedance values to be provided in a window 1035. This includes, for example, producing a complex impedance plot, as shown in Figure 6A. Alternatively the impedance values can be listed as shown in Figure 6B, or plotted as reactance verses frequency or resistance verses frequency as shown in Figures 6C and 6D respectively.

Frequency controls 1036 are provided to allow impedance measurements above or below threshold limits to be omitted from the displayed results, as shown by threshold markers 1037A, 1037B. Additionally a rejection limit can be applied to discard data points that fall outside a threshold variation from an idealised semi-circular locus provided on the complex impedance plot.

The impedance parameter values can then be analysed to derive indicators of hydration status.

In particular, as will be appreciated by persons skilled in the art, when a subject is undergoing dialysis, there is significant movement of fluid within the body. This can lead to an excess of extracellular fluid in some body segments, resulting in oedema, and/or a reduction in extracellular fluid in other body segments.

Accordingly, it is typical for the parameters to be used to derive indicators that are at least partially indicative of the extracellular fluid levels in each of the body segments and/or the entire body. The indicators are therefore typically indicative of the extracellular fluid volume, or an index based on the ratio of extra- to intra- cellular fluid.

In the case of the extracellular fluid volume, this can be calculated for each body segment using the equation:

$$ECV_{Segment} = C_{Segment}\rho_{Segment}\left(\frac{L^2_{Segment}}{R_{Segment}}\right) \quad (3)$$

Where ECV = Extracellular fluid volume

$C_{Segement}$ = Geometry Constant which is 1 for an arm or leg and 4 for the thoracic cavity

$L_{Segment}$ = Length of the segment in cm

$R_{Segment}$ = Resistance of the segment in Ohm

$\rho_{Segment}$ = Resistivity coefficient which is nominally 47 Ohm/cm

The resistivity coefficient can be determined at each moment by using a nominal population reference where alpha is measured and then a corresponding resistivity for extracellular fluid is determined. This can also be done using all the variables from a model such as the Cole model to determine the appropriate resistivity. Alternatively this can be manually entered or measured using techniques known to persons skilled in the art.

The total body fluid is calculated according to:

$$ECV_{Total} = 2(ECV_{arm} + ECV_{leg}) + ECV_{trunk} \quad (4)$$

The extracellular fluid resistance R_e is determined from:

$$R_e = R_0$$

and intracellular fluid resistance R_i is determined from:

$$R_i = \frac{R_\infty \mathrm{R_e}}{\mathrm{R_e} - R_\infty}$$

Thus, this can be used to derive an index I, which is indicative of the ratio of extra- to intra-cellular fluid is given by the equation:

$$I = \frac{R_i}{R_e} = \frac{R_\infty}{R_0 - R_\infty} \quad (5)$$

Additionally, the total body water can also be used as an indicator for hydration status. In this example, by positioning the electrodes as shown in Figure 8, this allows impedance measurements across the subject's entire body to be determined. This in turn allows the subject's total body water (TBW) to be derived given by:

$$TBW = ecf + icf \quad (6)$$

where: TBW = total body water
ecf = volume of extracellular fluid
icf = volume of intracellular fluid

In this regard, the volumes of extracellular and intracellular fluid can be derived from the values R_0, R_∞ as these depend on the values of the extracellular and intracellular resistance, as discussed above.

The analysis of the extracellular fluid volumes, the index I and/or the total body water may be achieved in a number of ways, but typically involves comparing the parameters to available references, and accordingly, the process determines if references are available at step 510. If references are available, the measuring device 1 allows the user to select an appropriate reference at step 520.

For example, the reference can be in the form of earlier data collected for the respective subject, thereby allowing a longitudinal analysis to be performed. This typically requires that data are collected prior to dialysis or other interventions, allowing the measuring device 1 to determine if there are any variations in the subject's extracellular fluid levels during the dialysis process, thereby indicating a change in subject hydration status. This can be performed for each body segment separately, or for the entire body.

However, the system may also or alternatively use a normal population database table, which includes reference values obtained from different subjects. This database table is essentially a single subject database table into which all measurements of normal population subjects (people without vascular insufficiency) are added.

An example of such normal population data displayed using the GUI 1000 is shown in Figure 7A. This table then acts as a pool of data from which normalised values for raw impedance data and ratios of impedance data can be generated, allowing comparison with measured values for the subject to be performed.

This generation of this normalised data is in the form of mean (averaged) values that are selected to be relevant to the test subject. The selection is performed based on the subject information and may be performed on the basis of any one of a number of factors, such as age, sex, height, weight, race, interventions, or the like.

Therefore if the test subject is female then the normalised data drawn from the normal population database will be calculated from measurements from female subjects that are present in the in the normal population database.

Thus, in one example, the operator is presented with the GUI 1040 similar to that shown in Figure 7A, which allows the operator to select appropriate records from the normal population table, as shown by the highlighted entry at 1041.

It will be appreciated that the normalised population references are generally less accurate than subject specific references as these do not necessarily accurately model the subject's fluid levels and hence hydration status prior to undergoing dialysis.

In the case of using a subject specific reference, this is generally achieved by ensuring measurements taken prior to surgery, requiring dialysis, interventions, heart disease, or other events that will have an impact on the hydration status. Thus, for example, if the subject is undergoing dialysis, then the reference can be formed from parameter values derived prior to commencement of the dialysis procedure.

A common example is baseline measurements taken before surgical intervention for breast cancer that can be used to track subjects fluid shifts post surgery by comparison of study measurements to these baseline generated mean values.

Subject specific baselines can be generated automatically from measurements in the subject's database table. This can in turn be used to provide cut off points for dialysis based on when the measured impedance values or derived indicators approach predetermined impedance or indicator values representing an ideal or optimal fluid level or hydration status.

Generation of baselines can be achieved using the GUI 1000 shown in Figure 7B, in which the subject's record is displayed. Located on the GUI 1000 are two selection windows 1042, 1043 that are used to define the measurements used from the subject's database table to generate mean data values for comparison to study measurements.

It will be appreciated that the process can also be used to add data to the normal population table. This is achieved by performing the measurement process outlined above, and in the event that the subject is healthy, or the subject is a control, such as a family member, importing the data into the normal population table. This can be performed in addition to adding the measurements to the subject record, so that measurements collected from a healthy individual can be used for subsequent longitudinal analysis and/or as a normal population reference.

In any event, once an appropriate reference is selected at step 520, the measuring device 1 compares the currently determined indicator to the reference at step 530, and utilises this to generate an indication of the hydrations status which is then displayed at step 540.

If no reference is available, the indicators determined for each body segment are compared to the indicators determined for other ones of the body segments. This allows a relative distribution of fluid within the subject to be monitored, which in turn allows an indication of hydration status to be determined.

For example, this can be used to determine the presence or absence of oedema. In the event that it is believed that the subject has one or more limbs at risk of oedema (i.e. suffering from vascular insufficiency of that limb), then the onset of oedema is in turn indicative of variations in the subject's hydration status. In this instance, the analysis of each of the limbs will be influenced by whether the subject is deemed to be at risk of bilateral oedema (i.e. suffering from vascular insufficiency of two limbs).

In particular, if there is no risk of bilateral oedema, then the processing system 10 can compare parameters for contra-lateral limbs. This may be achieved for example by determining an index based on a ratio of the extra- to intra- cellular fluid levels in each leg, and then comparing the values determined to assess whether there is difference between the limbs, or against a reference value for that limb, and hence whether there is a likelihood of oedema being present.

In the event that there is a likelihood of the vascular insufficiency being bilateral, then the processing system 10 typically determines the index for each limb. A ratio of the determined index I for different pairs of limbs are then compared, thereby allowing the operator to determine if there is a likelihood of bilateral oedema.

In any event, it can be seen that if there is a major variation in the extracellular fluid volume, or the index I, either over time in the case of longitudinal analysis (either extending through a dialysis session, or extending over multiple sessions), compared to normal references, or between different body segments, this is indicative of a changing hydration status. This is in turn indicative of the fact that the dialysis procedure needs to be modified in order to counteract this change, and ensure that the subject is correctly hydrated.

Accordingly, the measuring device 1 can use this to display a report that is indicative of the hydration status, and/or the presence, absence or degree of oedema.

However, as an alternative to the above described process, the hydration status can be monitored by examining other indicators, such as by examining the impedances values at different selected frequencies.

Thus, for example, this may involve calculating impedance values at specific frequencies in the complex impedance plot. This may include theoretical impedance values such as R_0 and R_∞, vectors representing the actual measured values, or theoretical values derived at set frequencies, as well as the difference between values of R_0 and R_∞.

In one example, the process set out in steps 510 to 540 can involve repeatedly making measurements during the dialysis procedure, and then monitoring the variation in one or more of the above mentioned indicators, such as the value of R_∞, the level of extra-cellular fluid, the index I, or the like.

In this example, as dialysis proceeds, fluid levels within the subject's body should alter, resulting in a corresponding alteration of the indicator. As the dialysis procedure reaches a desired end point and fluid levels within the subject approach an ideal or optimal level, this will also result in a corresponding stabilisation of the indicators. Accordingly, in one example, the process involves monitoring for variation, and in particular, a rate of change of the indicators. When the rate of indicator variation falls below a predetermined threshold, this indicates that the value of the indicator, and hence patient fluid levels, have substantially stabilised, thereby allowing the dialysis procedure to be halted.

Thus, in one example, the process involves monitoring changes in the values of indicators such as R_0, R_∞, the difference between R_0 and R_∞, vector impedance values, or any other indicator, and then using the rate of variation to control the dialysis process.

Examples of the different types of available reports will now be described with reference to Figures 7C to 7I.

As shown in Figure 7C, the report is presented using a GUI 1050 that includes subject details shown generally at 1051. The GUI includes controls 1052 that allow the operator to select whether reference data is to be used and the nature of the reference data. Thus, it will be appreciated that if a user varies the reference data selection, the process will return to step 540 to reassess the nature of the output dependent on the type of reference selected. At 1053A a drop down list is provided to indicate the nature of the parameter that is to be displayed, and at 1053B checkboxes are provided indicating the limbs for which the parameter is to be displayed. In addition to this, a limb of interest and a reference limb can be selected using the check boxes 1054, 1055 as shown.

The parameters available for charting include:

- Weight;
- Fluid loading;
- Ratio of indices;
- Ratio of body segment R_0 values;
- The index for each individual body segment R_0 for a body segment;
- R_∞ for a body segment;
- The intracellular fluid resistance R_i;
- The characteristic frequency of the subject f_c;
- Standard error of estimates;
- *Td* time delay for each measurement; and,
- Values of α and τ from the Cole Model.

Each of the parameters will now be described in more detail.

Fluid Loading

The impedance vector plot is a graphical representation of when a subject's measurements move relative to a reference ellipse. The reference ellipse can be generated from a 95% confidence interval based on the subject specific baseline data or the normal population data.

When data points of a study body segment are outside the ellipse, this indicates the presence of too much fluid in the corresponding body segment. The ellipse can be generated for and displayed for each body segment chosen using the reference limb checkbox. The data points displayed are those generated from the study body segment data for the subject. The study body segments and reference body segments are chosen using the body segment selector check boxes located underneath the chart.

Figure 7C shows an example of a fluid loading plot in which the index for left and right legs is compared. In this example, the index remains within the ellipse shown generally at 1056 highlighting that oedema is not present, and optimum dry mass has been obtained. However, when the right arm and left arm are compared as shown in Figure 7D, the values for the ratio comparisons fall outside the reference ellipse 1056 indicating that the right arm is suffering from fluid overload and may have vascular insufficiency.

In these examples, the fluid loading plot includes a comparison between limbs, and accordingly, the checkboxes 1053B are not used.

An alternative example is shown in Figure 7I. In this example, the reference ellipse is replaced by reference lines 1071, 1072, defining a "funnel" shaped reference region 1070. In this example, the reference region may again be based on a 95% confidence interval from the subject's specific baseline data or the normal population data.

In contrast to the reference ellipse of Figures 7C and 7D above, the reference region 1070 is generally more able to take into account variations in physical characteristics between subjects. For example, when a reference ellipse is determined based on population samples, then if a subject has particularly thin limbs, or short fat limbs, then the subject's measured value may fall outside the ellipse, even when the hydration status is normal. However, this does not occur with the reference region 1070.

A further benefit is that if the subject has some form of oedema and is over hydrated, then this will result in the measured index value that is positioned below the reference line 1072, as shown for example at 1073.

If the measured index is determined to be above the line 1071, as shown for example at 1074, this generally indicates either that the patient is dehydrated, which will require further clinical intervention, or investigation. Alternatively, this indicates that the electrodes have been incorrectly attached to the subject, in which case re-measurement may be required.

Ratio of body segment Indices

This will display the index I for a selected reference limb divided by the index I of the limb of interest.

Figure 7E is an example of the ratio of limb ratios in which a ratio of the index for the right arm and right legs is plotted against time. In this instance, it can be seen that a significant variation is present at 1057 indicating an undesirable fluid loading.

In this examples, as two limbs are again compared, the checkboxes 1053B are not used, and are ignored.

Ratio of body segments R_0 values

This function will display the ratio of the R_0 of the reference body segment divided by that of a study body segment for each measurement in the subject's database table.

Index I for each body segment

The index *I* can also be displayed for each body segment for all measurements in the subjects database table as a chart over time, as shown in Figure 7F. The body segments represented on the chart are selected using the control 1053. In this instance, as reference and study limbs are not defined, the 1054, 1055 are omitted for clarity.

Resistance at zero kHz (R_0) for a single body segment

The value of R_0 can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Resistance at infinite frequency (R_∞) for a single body segment

The value of R_∞ can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Resistance for the intracellular fluid (R_i) for a single body segment

The value of R_i can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Characteristic frequency for single body segment

The characteristic frequency can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Value of α and τ from the Cole Model

The value of α and τ can also displayed for each body segment for all measurements in the subject's database table as a chart over time.

SEE (standard estimate of errors) values for a single body segment

The value of the standard estimate of errors (SEE) can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Td (time delay) values for a single body segment

The value of the time delay (*Td*) associated with each measurement can also displayed for each body segment for all measurements in the subjects database table as a chart over time.

Reference Indications

In each of the above outlined reports, reference values can also be displayed based either on the normalised population reference or subject specific reference.

An example of the use of a subject's specific reference value is shown in Figure 7F. In this instance the reference value is based on R_0 as shown at 1058. Accordingly, it can be seen that variation of the value R_0 compared to the reference is indicative of oedema. The generation of a report by comparison to normal population data will be performed in a similar manner.

In addition to simply displaying the absolute reference value determined, it is also possible to display standard deviations as shown at 1059 to thereby provide an indication of the degree of variation from the base line.

Event Markers

A further feature of the process is the ability to associate event markers with specific measurements in the measurement database table. Event markers can provide commented time points that correspond to measurements and points in time. These can be customised by the user to indicate important events that need to be documented on the longitudinal analysis charts. Such events may include, onset date of oedema, the start of medical intervention, the beginning and end of dialysis sessions etc. These markers will be displayed automatically on the longitudinal charts that are a function over time. Event markers can also be shown on charts as shown for example in Figure 7H.

Alternative Analysis

In the above examples, the processing system 10 therefore selects the types of analysis or representation that is most appropriate for determining the presence or absence of oedema based on the currently available data. This therefore removes the requirement for the operator to make an assessment of which form of report would provide the most accurate indication of the onset of oedema.

In the above example, the impedance measurements are collected for each of the limbs, with the assessment of the preferred type of analysis being performed after the measurements have been performed. However, as an alternative to this, the processing system 10 can be adapted to determine the preferred type of analysis first and then only perform the measurements required in order for the type of analysis to be performed.

Thus a limited limb analysis can be performed, in which the operator specifies the limbs for which measurements are to be made prior to the measurement process. In this instance, data will only be collected for the limbs of interest.

In addition to performing the measurements described above, it is possible that profiles can be configured to allow a range of different measurements to be performed.

For example, the TBW can be used in:

- body composition analysis
- derivation of Fat Free Mass (FFM), which can in turn be used as an index of left ventricular mass;
- monitoring the build up of fluid in the body of cardiac patients, which can be used as an indicator of right ventricular failure.

Furthermore, by subtracting measured impedance values obtained for each limb from the corresponding impedance values obtained for the entire body, this can be used to derive effective thoracic cavity impedance values. These values can in turn be used as indicators for pulmonary oedema, and hence left ventricular failure, as well as determining cardiac output.

Thus, it will be appreciated that in addition to measuring hydration status, different measurement profiles can be determined to allow measurement of:

- Cardiac parameters;
- Pulmonary oedema;
- Lymphoedema;
- Body composition; and,
- Total body water.

Remote Computer System

The above examples have been described on the basis of the selection of the preferred impedance measurements and analysis being performed by a processing system 10 provided as part of the measuring device. However, this is not essential and that any or all of the functionality described could be performed by a processing system that is remotely located to the measuring device, as will now be described with respect to Figure 9.

In this example, the measuring device 1 (which is shown as a single channel device for clarity purposes only) is connected to a computer system 3, via the external interface 23 as shown. The computer system 3 may be any form of computer system but is typically a desktop, laptop, tablet, PDA, Smart Phone or the like.

In this example, the computer system 3 operates to control the measuring device 1 to perform the measurement procedure. The measuring device 1 therefore operates to generate required excitation signals, apply these to the subject, and measure the resulting voltages generated across the subject. Once impedance measurements have been collected, these are transferred via the external interface 23

to the end station 3, which operates to analyse the measured impedance values and generate the appropriate GUIs shown in Figures 5 to 8.

In order to achieve this, the computer system 3 may be connected to the measuring device 1 via a wired, or wireless connection, or alternatively via an appropriate communications network 5, such as an Ethernet, LAN, WAN, the Internet, or the like.

In this instance, the operator of the system is generally required to place the measuring device 1 in a predetermined operating mode allowing the computer system 3 to generate any required control signals to activate the measurement process.

In this example, communication between the computer system 3 and the measuring device 1 is typically controlled using the GUI 1060 shown in Figure 10.

The GUI includes fields 1061 for defining IP connection details, which allows the computer system 3 to connect to the measuring device, via the external interface 23, via a TCP/IP or other network. Fields 1062 are used for defining paths via which the references can be obtained, with the fields 1063 defining details of the database from which the references should be obtained.

Fields 1064 and 1065 are used to define parameters relating to the impedance analysis to be performed, including default frequency, rejection and time delay limits, as well as reference ranges or the like. Finally fields 1066 are used to define properties of the resulting analysis report.

It will therefore be appreciated from this that GUI can also be used to provide connections to remote databases, such as HL7 compliant subject databases. Furthermore, the architecture can be implemented in any one of a number of manners depending on the circumstances in which the measuring device 1 is to be used.

Thus, for example, as a further alternative, the selection and/or analysis of the impedance measurements can be performed by a central base station coupled to a number of measuring devices via a suitable communications system, such as a computer network or the like. In this instance, once the base station has selected an impedance measurement type to be performed, the base station transfers an indication of this to the respective monitoring thereby causing the measuring device to display the necessary electrode connections. Once the impedance measurements have been performed, the determined measurements are returned to the base station for analysis.

Patient Orientation

It will be appreciated that the location of fluid within a subject will vary significantly as the subject moves, and in particular as the subject changes their orientation or posture.

For example, in performing dialysis it is typical for the subject to be seated in a relined position, in which case fluid is typically distributed unevenly throughout the body (and subject to any specific oedema or the like). If the subject were to stand up or lay down during the process, this results in a significant flow of fluid into or from the lower regions of the subject, such as the calf. Consequently, if measurements are made from the calf, there can be a significant variations in measured impedances associated with the subject's position.

To take this into account, the measuring device 1 may include an orientation sensor connected to the measuring device 1 as a peripheral device 4, for example. In this instance, the orientation sensor is used to derive information regarding the subject's current orientation, and this could therefore take on any one of a number of forms.

Thus, for example, the orientation sensor could be provided in a subject's bed and operate to determine the subject's orientation based on the bed configuration. Alternatively, the orientation sensor may be coupled to the subject, and in particular to the subject's leg or calf, to determine the leg or calf orientation. It will be appreciated from this that any suitable sensor may be used, and in one example, the sensor is at least partially incorporated into the electrodes 15.

In use, the measuring device 1 can modify the impedance measurement analysis based on the orientation of the subject as determined from the orientation sensor. This can again be achieved in a number of manners.

For example, if the measuring device 1 is comparing a current indication to a previous indication, such as by monitoring variations in the index I over time, the measuring device 1 can be adapted to ensure that indications are only compared to each other if made at the same subject orientation. Thus, if a preliminary impedance measurement prior to dialysis is used to establish a baseline reading, with subsequent measurements being compared thereto, the process may involve taking a baseline reading at each of a number of different orientations. In this instance, the measured readings would then be compared to the corresponding baseline determined for the same subject orientation. The fluid levels will also depend on the length of time a subject has been in a given orientation, and again this may be taken into account, for example, by ensuring comparison is made to prior readings in which the subject has maintained a similar posture for a similar amount of time.

Alternatively, by measuring different impedance values obtained over a range of orientations, this can be used to determine a correction factor, required to correct for certain orientations. This allows normalisation of any measured values to a specific orientation, allowing the above described analysis to be performed.

A further variation is to examine differences in indicators between different subject orientations. In this instance, it will be appreciated that if the subject's hydration status is such that the subject has reached an ideal or optimal fluid level, and no further dialysis is required, then changes in orientation will have a reduced effect simply because there is less fluid within the body to be displaced.

Accordingly, in a further example, the process involves determining a number of indicators at different subject orientations. The measuring device 1 then compares the measured indications at each orientation and determines if the difference falls below a threshold. If so, then this indicates that there is minimal variations in fluid between the orientations, and hence that the hydration status is suitable to terminate the dialysis procedure.

Skin Temperature

Impedances values measured for a subject include a contribution from the subject's skin, known as a skin impedance. The skin impedance is heavily influenced by the hydration levels in the skin, which is in turn dependent on skin temperature.

Accordingly, in a further example, the measuring device 1 can use the skin temperature of the subject when analysing impedance values. This can be achieved in a number of ways.

For example, the skin temperature can be measured using a suitable thermometer, with the skin temperature being supplied to the measuring device 1, via the I/O device 22. Alternatively, a skin temperature sensor can be provided as part of the measuring device, either as a peripheral device 4, or through incorporation into suitable electrodes, allowing the measuring device 1 to determine the subject's skin temperature automatically.

In this example, the skin temperature is generally used to generate a calibration factor, which is used to modify the measured impedance values, or subsequently determined indicators, depending on the skin temperature. The calibration factor is typically predetermined by analysis of a suitable sample population, across a variety of skin temperatures.

An effect of the calibration factor is that it can be used to take into account subject ethnicity. In particular, it is generally accepted that different reference baselines must be used for subjects having different ethnicities, due to variations in skin impedance. However, by providing a correction factor

taking into account both ethnicity and skin temperature, allows common baselines to be used by a wider range of subjects having a wider range of ethnicities.

Electrode Arrangement

It will be appreciated that the above described electrode arrangements are only one of a number of possible electrode arrangements. For example, whilst the electrodes may be provided as discrete pads, alternatively a number of electrodes may be provided on a common substrate, for example in the case of band electrodes.

Additionally, or alternatively, the electrodes may form part of another related device. For example, the voltage measuring electrodes positioned on either the calf or bicep can be incorporated into blood pressure cuff, to allow simultaneous measurement of blood pressure and impedance.

In any event, it will be appreciated that the above described process provides an easy to use and non-invasive estimate of body composition parameters and fluid volumes. Segmental analysis provides a better estimate of these parameters then traditional whole body estimates. However the placement of electrodes in reproducible anatomic sites in the obese and the critically ill population is often impossible. By using the theory of equipotentials and sophisticated multiplexing it is possible to provide a robust bioimpedance platform capable of multiple measurement parameters for the dialysis patient.

Persons skilled in the art will appreciate that numerous variations and modifications will become apparent. All such variations and modifications which become apparent to persons skilled in the art, should be considered to fall within the spirit and scope that the invention broadly appearing before described.

Thus, for example, it will be appreciated that features from different examples above may be used interchangeably where appropriate. Furthermore, whilst the above examples have focussed on a subject such as a human, it will be appreciated that the measuring device and techniques described above can be used with any animal, including but not limited to, primates, livestock, performance animals, such race horses, or the like.

It will also be appreciated above described techniques, may be implemented using devices that do not utilise the separate first processing system 10 and second processing system 17, but rather can use a common single processing system, or use some other internal configuration.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1) A method of determining an indication of the hydration status relating to a subject, the method including, in a processing system:
   a) determining a measured impedance value for at least one body segment;
   b) for each body segment, and using the measured impedance values, determining at least one indicator, the indicator being at least partially indicative of a level of extracellular fluid;
   c) determining an indication of the hydration status using at least one determined indicator.

2) A method according to claim 1, wherein the method includes, in the processing system:
   a) comparing the at least one indicator to at least one of:
      i) a predetermined reference;
      ii) an indicator determined for at least one other body segment; and,
      iii) a previously determined indicator; and,
   b) determining an indication of the hydration status using the results of the comparison.

3) A method according to claim 2, wherein the reference includes at least one of:
   a) a predetermined threshold;
   b) a tolerance determined from a normal population;
   c) a predetermined range; and,
   d) an indicator previously determined for the subject.

4) A method according to any one of the claims 1 to 3, wherein the indicator is at least one of:
   a) an index (*I*)of the ratio of extra- to intra-cellular fluid; and,
   b) an extracellular fluid volume.

5) A method according to any one of the claims 1 to 4, wherein the method includes, in the processing system:
   a) determining a plurality of measured impedance values for each body segment, each measured impedance value being measured at a corresponding measurement frequency; and,
   b) determining impedance parameter values based on the plurality of measured impedance values, the indicator being at least partially based on the determined impedance parameter values.

6) A method according to claim 5, wherein the parameter values include R_0 and R_∞ wherein:
   R_0 is the resistance at zero frequency; and,
   R_∞ is the resistance at infinite frequency.

7) A method according to claim 6, wherein the method includes:
   a) monitoring changes over time for at least one of:
      i) R_0;
      ii) R_∞;

iii) a difference between R_0 and R_∞;

b) a vector indication of an impedance measurement.

8) A method according to claim 6, wherein the method includes, in the processing system:

a) determining values for parameters R_0 and R_∞ from the measured impedance values; and,

b) determining the indicator by calculating the index (I) using the equation:

$$I = \frac{R_\infty}{R_0 - R_\infty}$$

9) A method according to claim 6, wherein the method includes, in the processing system, determining the parameter values using the equation:

$$Z = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega\tau)^{(1-\alpha)}}$$

where:

Z is the measured impedance at angular frequency ω,

τ is a time constant, and

α has a value between 0 and 1.

10) A method according to claim 9, wherein the method includes, in the processing system:

a) determining the impedance of each body segment at four discrete frequencies; and,

b) determining values for the parameters by solving the equation using four simultaneous equations.

11) A method according to claim 6, wherein the method includes, in the processing system, determining the parameter values by:

a) determining a complex impedance locus using the measured impedance values; and,

b) using the complex impedance locus to determine the parameter values.

12) A method according to any one of the claims 1 to 11, wherein the indicator for a body segment is the extracellular fluid volume determined using the equation:

$$ECV_{Segment} = C_{Segment}\rho_{Segment}\left(\frac{L^2_{Segment}}{R_{Segment}}\right)$$

Where ECV = Extracellular fluid volume

$C_{Segement}$ = Geometry Constant which is 1 for an arm or leg and 4 for the thoracic cavity

$L_{Segment}$ = Length of the segment in cm

$R_{Segment}$ = Resistance of the segment in Ohm

$\rho_{Segment}$ = Resistivity coefficient which is nominally 47 Ohm/ cm

13) A method according to claim 12, wherein the method includes determining an indicator for the entire body the equation:

$$ECV_{Total} = 2(ECV_{arm} + ECV_{leg}) + ECV_{trunk}$$

14) A method according to any one of the claims 1 to 13, wherein the second body segment and the at least one other body segment are different types of body segment.

15) A method according to any one of the claims 1 to 14, wherein the body segments are limbs.

16) A method according to claim 15, wherein the body segment includes at least one of:

a) a calf; and,

b) a bicep.

17) A method according to any one of the claims 1 to 16, wherein the method includes, in the computer system:

a) determining a correction factor; and

b) determining the hydration status using the correction factor.

18) A method according to claim 17, wherein the correction factor is indicative of at least one of:

a) a subject orientation or posture;

b) a subject skin temperature; and,

c) a subject ethnicity.

19) A method according to any one of the claims 1 to 18, wherein the method includes, in the computer system:

a) determining a subject orientation; and

b) determining the hydration status using the orientation.

20) A method according to any one of the claims 1 to 19, wherein the method includes, in the computer system:

a) determining a first indicator at a first subject orientation;

b) determining a second indicator at a second subject orientation; and

c) determining the hydration status using the difference between the first and second indicators.

21) A method according to any one of the claims 1 to 20, wherein the method includes, in the computer system:

a) determining a first indicator at a first time;

b) determining a second indicator at a second time; and

c) determining the hydration status using the difference between the first and second indicators.

22) A method according to any one of the claims 1 to 21, wherein the method includes, in the computer system, displaying an indication of at least one of:

a) parameter values;

b) the indicator;

c) an extracellular fluid volume; and,

d) a ratio of extra-cellular to intra-cellular fluid.

23) A method according to any one of the claims 1 to 22, wherein the method includes, in the processing system:

a) receiving data representing at least one measured impedance value; and,

b) generating a representation of the at least one measured impedance value.

24) A method according to claim 23, wherein the method includes, in the processing system:

a) selecting a representation type based on a selected impedance measurement type; and,

b) generating the representation in accordance with the selected representation type.

25) A method according to claim 23, wherein the representation is in the form of at least one of:

a) a Complex impedance plot;

b) an argand diagram;

c) a list of impedance values;

d) a reactance against frequency plot; and,

e) resistance against frequency plot.

26) A method according to any one of the claims 1 to 25, wherein the method includes, in the processing system:

a) receiving data representing at least one measured impedance value;

b) processing the at least one measured impedance value to determine at least one impedance parameter; and,

c) generating a representation of the at least one impedance parameter.

27) A method according to any one of the claims 1 to 26, wherein the method includes, in the processing system:

a) causing one or more electrical signals to be applied to the subject using a first set of electrodes, the one or more electrical signals having a plurality of frequencies;

b) determining an indication of electrical signals measured across a second set of electrodes applied to the subject in response to the applied one or more signals;

c) determining from the indication and the one or more applied signals, an instantaneous impedance value at each of the plurality of frequencies; and,

d) determining the indicator using the instantaneous impedance values.

28) A method according to claim 27, wherein the electrodes are positioned in accordance with the theory of equal potentials.

29) A method according to claim 28, wherein the positioning of the electrodes includes:

a) a first current supply electrode positioned on a limb being measured;

b) a second current supply electrode on a second limb on a the same lateral side of the subject as the limb being measured;

c) a first voltage electrode positioned on a limb being measured; and,

d) a second voltage electrode positioned on a third limb contra-lateral to the limb being measured.

30) A method according to any one of the claims 1 to 29, wherein the processing system is coupled to a measuring device, and wherein the method includes, in the processing system:

a) generating instructions; and,

b) transferring the instructions to the measuring device, the measuring device being responsive to the instructions to cause the impedance measurements to be performed.

31) A method according to any one of the claims 1 to 29, wherein the processing system forms part of a measuring device.

32) A method according to claim 29 or claim 30, wherein the measuring device includes at least two channels, each channel being adapted to measure the impedance across a respective body segment, and wherein the method includes, in the processing system, causing at least one impedance measurement to be performed using each channel.

33) A method according to claim 30, wherein the measuring device includes a processor, and wherein the processor is for:

a) receiving the instructions; and,

b) causing one or more impedance measurements to be performed using the instructions.

34) Apparatus for detecting tissue oedema in a subject, the apparatus including a processing system for:

a) determining a measured impedance value for at least one body segment;

b) for each body segment, and using the measured impedance values, determining at least one indicator, the indicator being at least partially indicative of a level of extracellular fluid;

c) determining an indication of the hydration status using at least one determined indicator.

35) Apparatus according to claim 34, wherein the apparatus includes:

a) a current supply for generating an alternating current at each of a plurality of frequencies;

b) at least two supply electrodes for applying the generated alternating current to a subject;

c) at least two measurement electrodes for detecting a voltage across the subject; and,

d) a sensor coupled to the measurement electrodes for determining the voltage, the sensor being coupled to the processing system to thereby allow the processing system to determine the measured impedances.

36) Apparatus according to claim 34, wherein the apparatus is adapted to perform the method of any one of the claims 1 to 33.

37) A method for use in dialysis of a subject, the method including, in a processing system:

a) determining one or more impedance values for at least one body segment;

b) for each body segment, and using the measured impedance values, determining at least one indicator; and,

c) selectively controlling the dialysis the subject using at least one determined indicator.

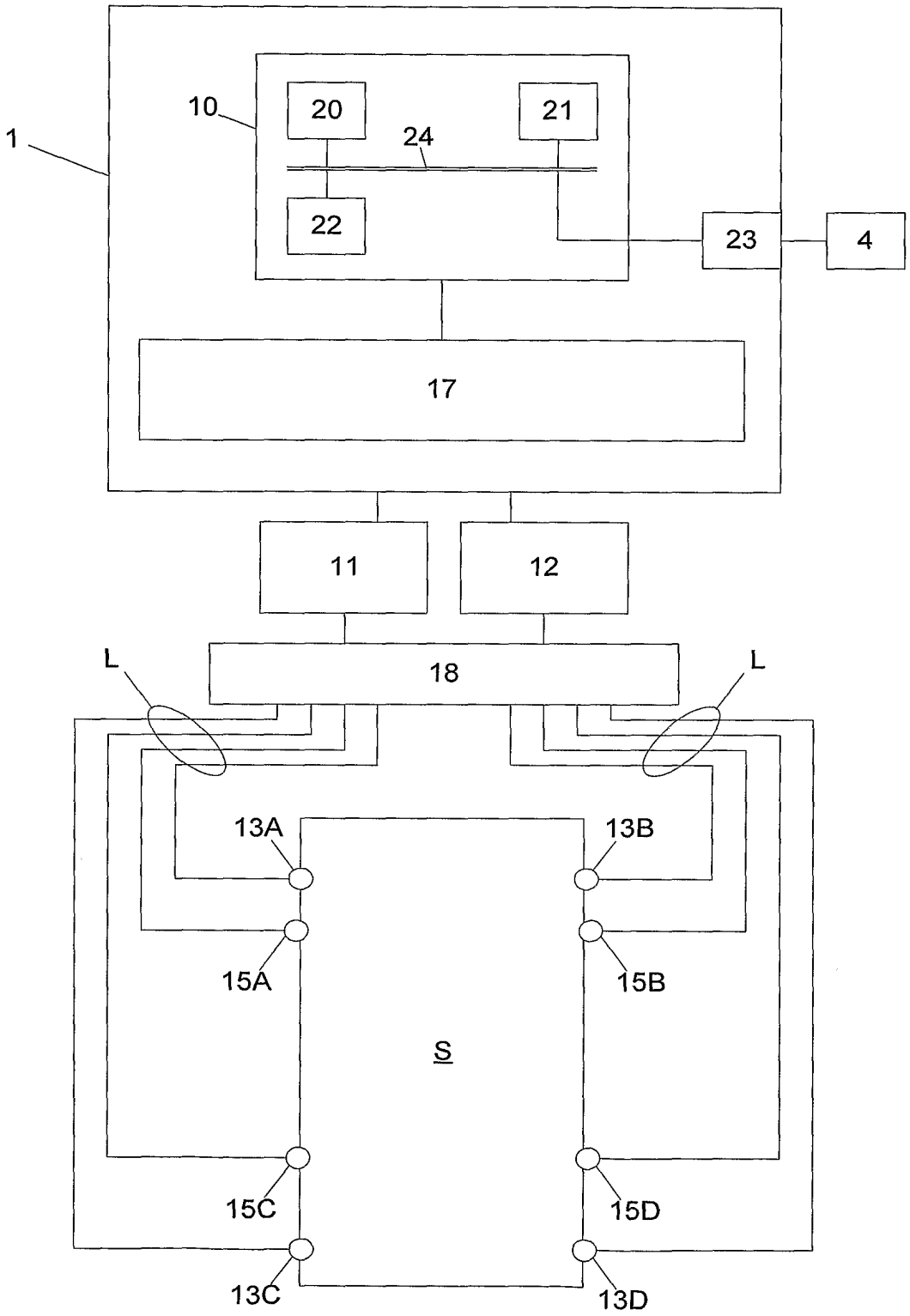

Fig. 1

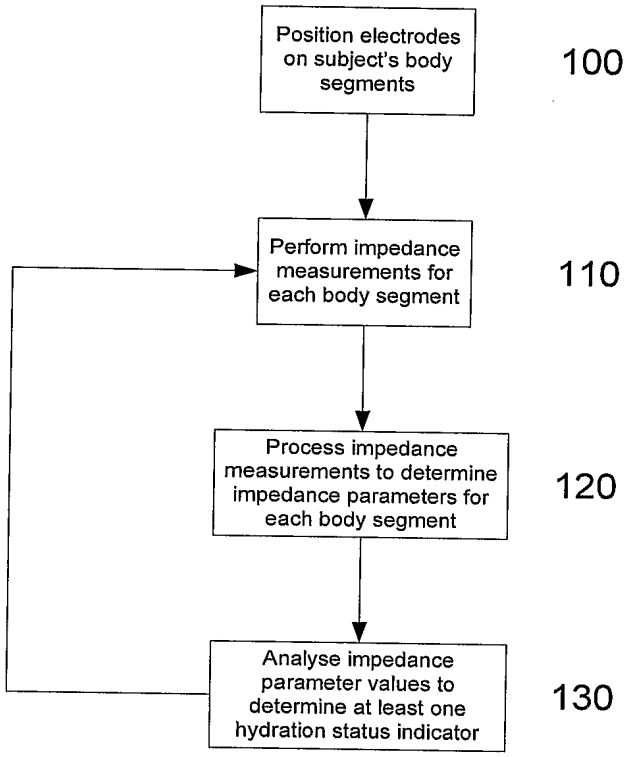
Position electrodes on subject's body segments
100
Perform impedance measurements for each body segment
110
Process impedance measurements to determine impedance parameters for each body segment
120
Analyse impedance parameter values to determine at least one hydration status indicator
130

Fig. 2

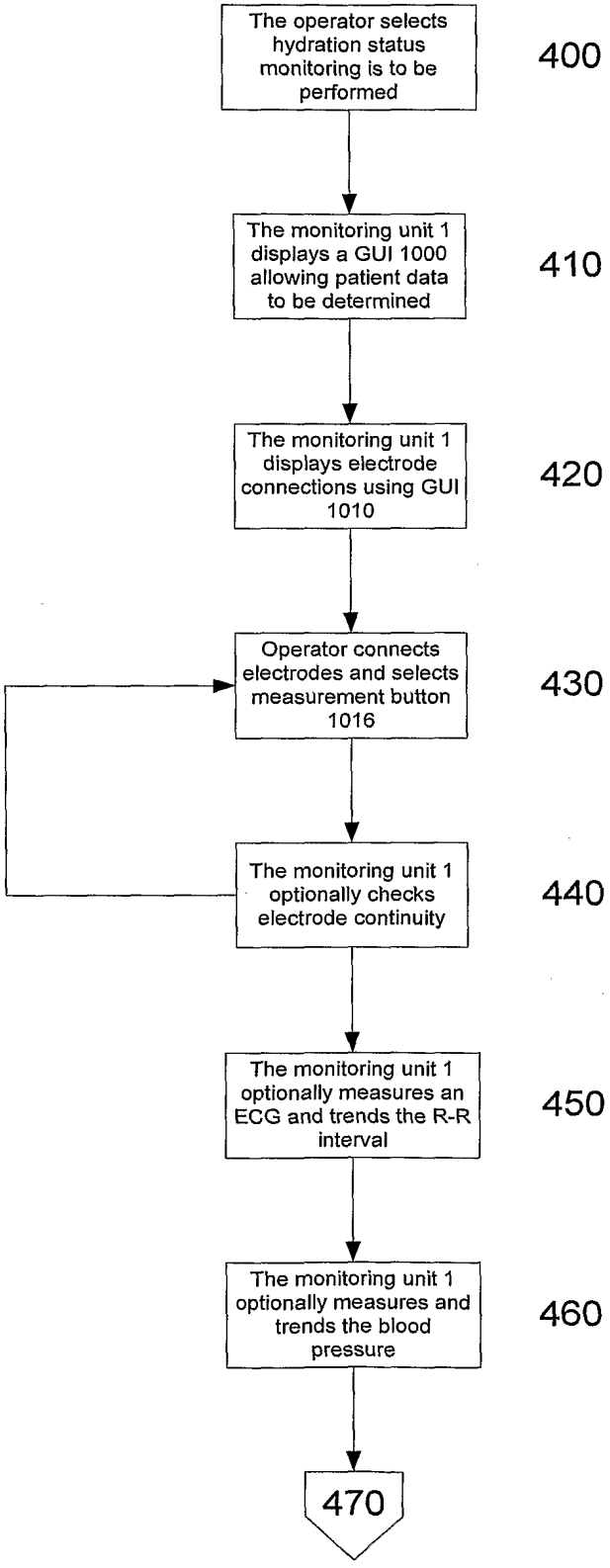
The operator selects hydration status monitoring is to be performed
400
The monitoring unit 1 displays a GUI 1000 allowing patient data to be determined
410
The monitoring unit 1 displays electrode connections using GUI 1010
420
Operator connects electrodes and selects measurement button 1016
430
The monitoring unit 1 optionally checks electrode continuity
440
The monitoring unit 1 optionally measures an ECG and trends the R-R interval
450
The monitoring unit 1 optionally measures and trends the blood pressure
460
470

Fig. 3A

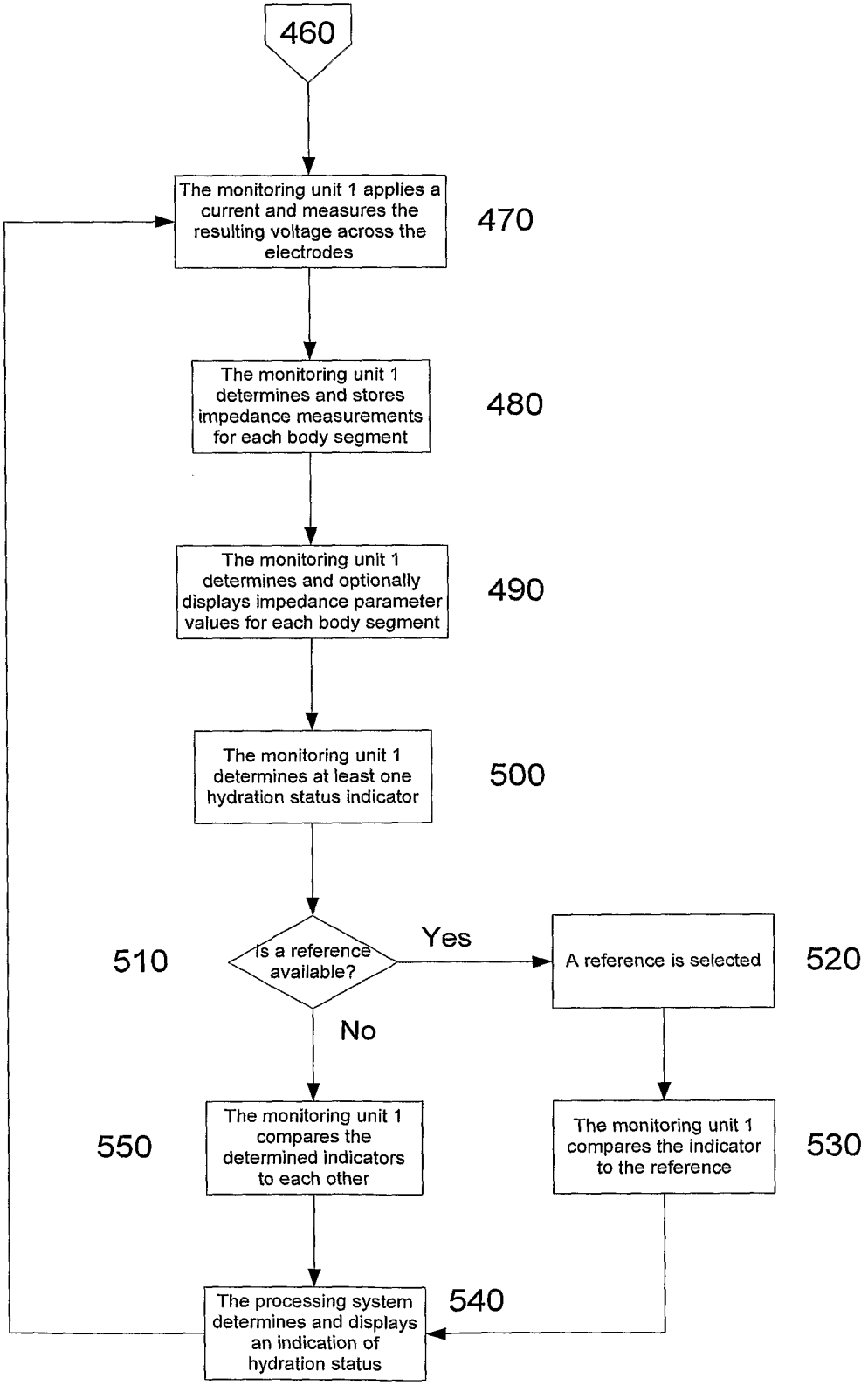
460
The monitoring unit 1 applies a current and measures the resulting voltage across the electrodes
470
The monitoring unit 1 determines and stores impedance measurements for each body segment
480
The monitoring unit 1 determines and optionally displays impedance parameter values for each body segment
490
The monitoring unit 1 determines at least one hydration status indicator
500
510
Is a reference available?
Yes
A reference is selected
520
No
550
The monitoring unit 1 compares the determined indicators to each other
The monitoring unit 1 compares the indicator to the reference
530
The processing system determines and displays an indication of hydration status
540

Fig. 3B

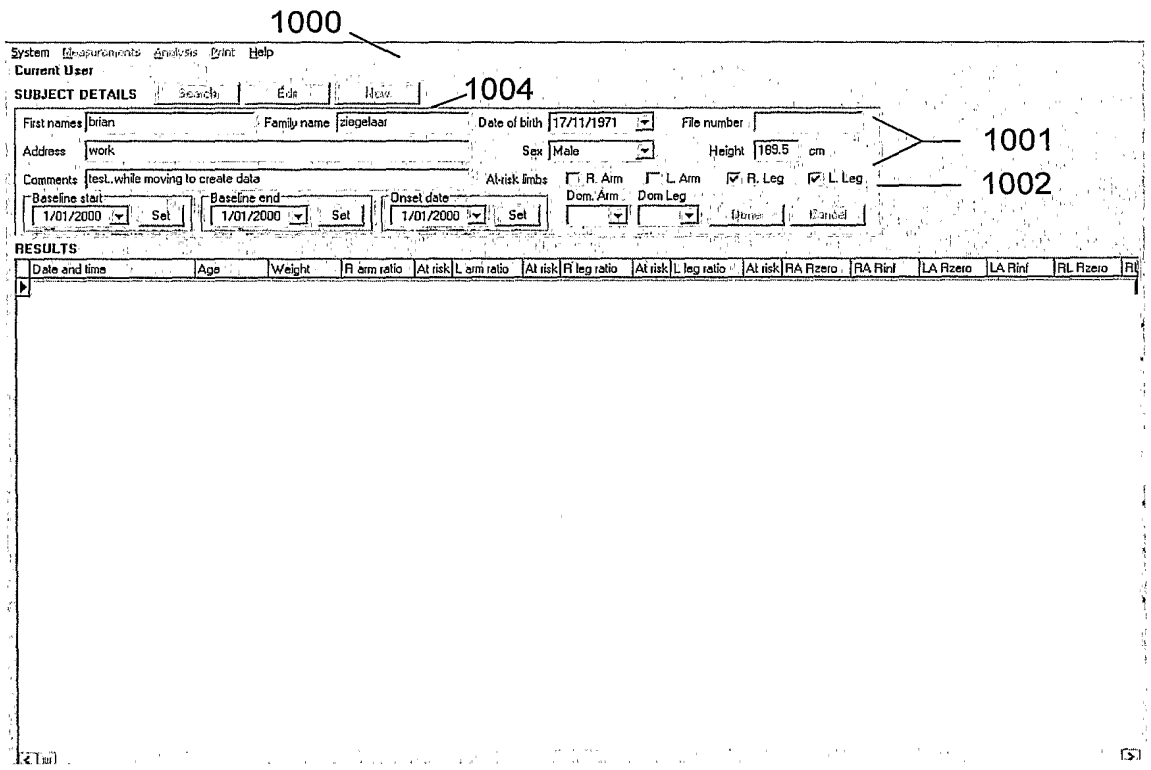
1000
System Measurements Analysis Print Help
Current User
SUBJECT DETAILS
Search
Edit
New
1004
First names brian
Family name ziegelaar
Date of birth 17/11/1971
File number
Address work
Sex Male
Height 169.5 cm
1001
Comments test..while moving to create data
At-risk limbs
R. Arm
L. Arm
R. Leg
L. Leg
1002
Baseline start
1/01/2000
Set
Baseline end
1/01/2000
Set
Onset date
1/01/2000
Set
Dom. Arm
Dom Leg
Done
Cancel
RESULTS
Date and time
Age
Weight
R arm ratio
At risk
L arm ratio
At risk
R leg ratio
At risk
L leg ratio
At risk
RA Rzero
RA Rinf
LA Rzero
LA Rinf
RL Rzero

Fig. 4A

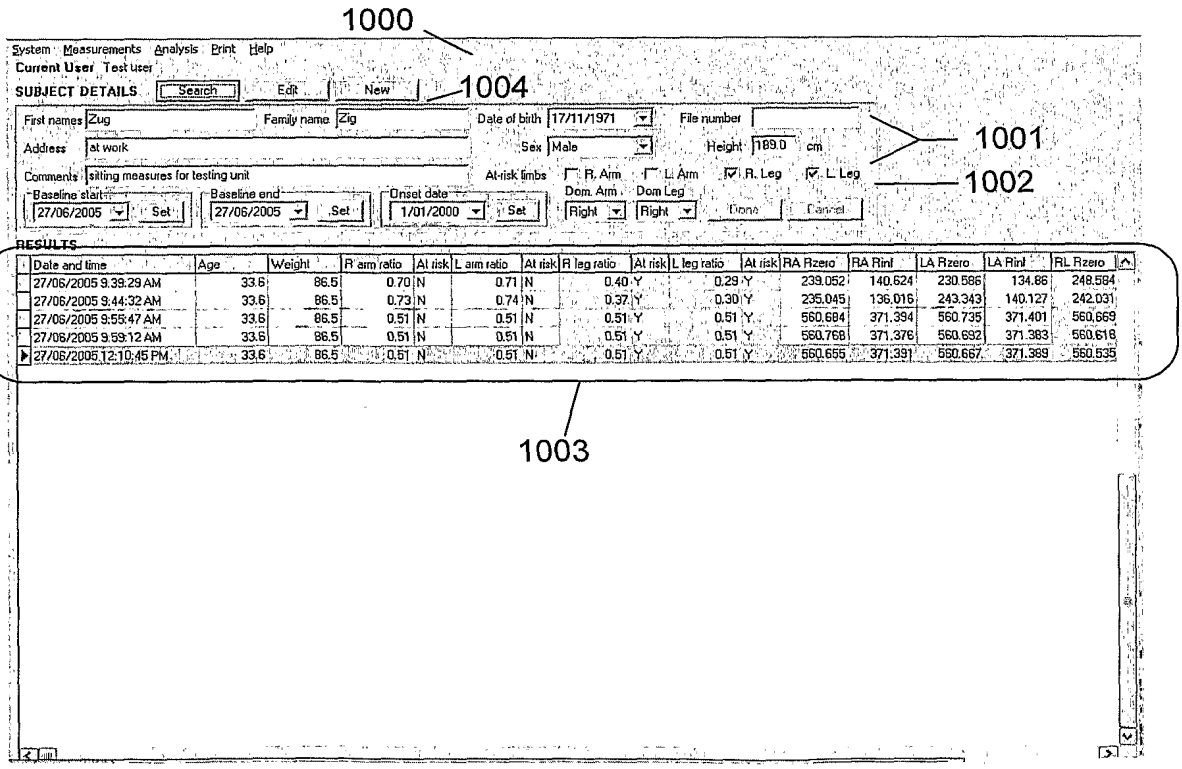
1000
System Measurements Analysis Print Help
Current User Test user
SUBJECT DETAILS
Search
Edit
New
1004
First names Zug
Family name Zig
Date of birth 17/11/1971
File number
Address at work
Sex Male
Height 189.0 cm
1001
Comments sitting measures for testing unit
At-risk limbs
R. Arm
L. Arm
R. Leg
L. Leg
1002
Baseline start
27/06/2005
Set
Baseline end
27/06/2005
Set
Onset date
1/01/2000
Set
Dom. Arm
Right
Dom Leg
Right
Done
Cancel
RESULTS
Date and time
Age
Weight
R arm ratio
At risk
L arm ratio
At risk
R leg ratio
At risk
L leg ratio
At risk
RA Rzero
RA Rinf
LA Rzero
LA Rinf
RL Rzero
27/06/2005 9:39:29 AM 33.6 86.5 0.70 N 0.71 N 0.40 Y 0.29 Y 239.052 140.624 230.586 134.86 248.584
27/06/2005 9:44:32 AM 33.6 86.5 0.73 N 0.74 N 0.37 Y 0.30 Y 235.045 136.016 243.343 140.127 242.031
27/06/2005 9:55:47 AM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.684 371.394 560.735 371.401 560.669
27/06/2005 9:59:12 AM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.768 371.376 560.692 371.383 560.618
27/06/2005 12:10:45 PM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.655 371.391 560.667 371.389 560.535
1003

Fig. 4B

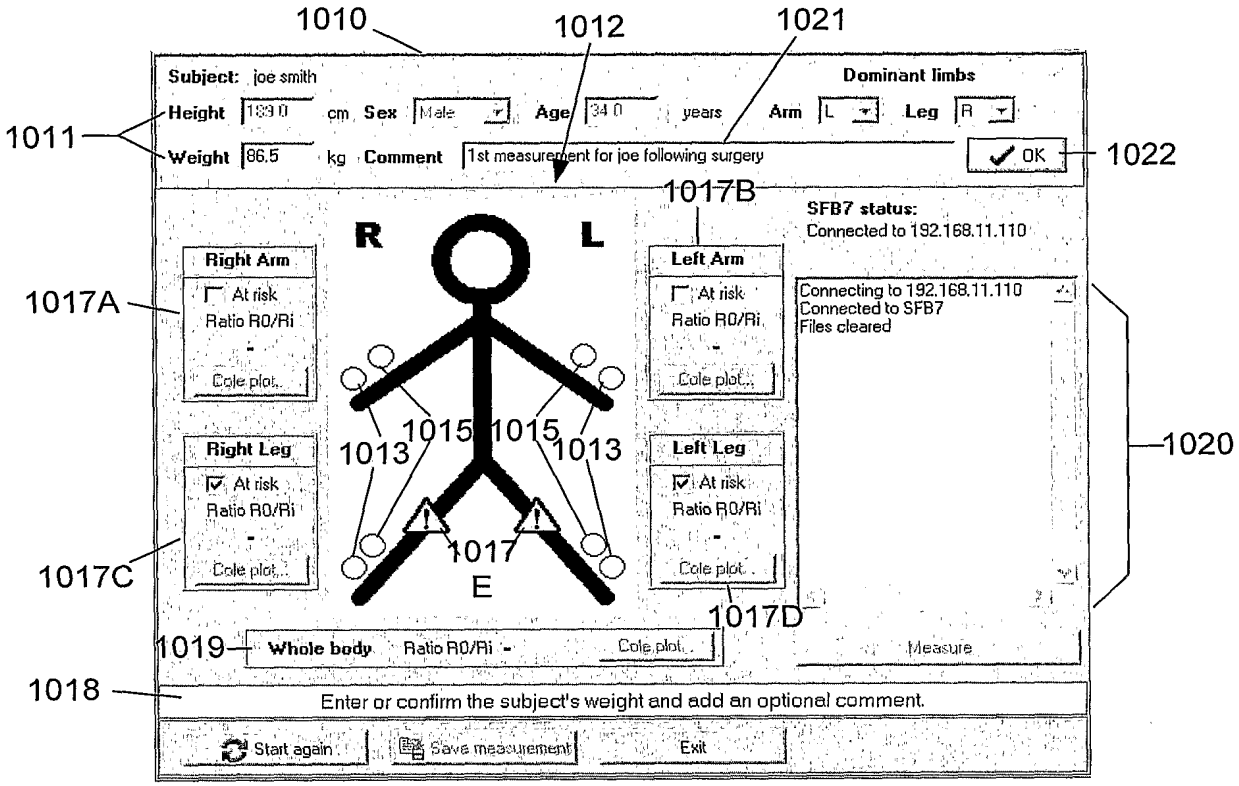

Fig. 5A

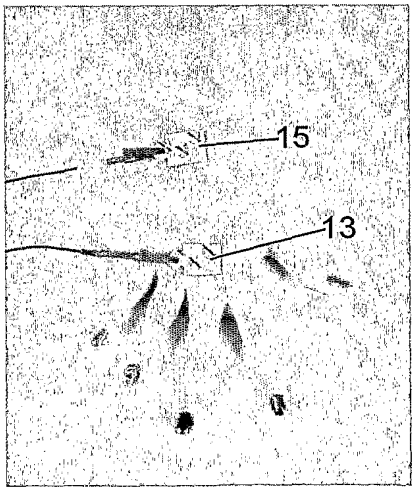

Fig. 5B

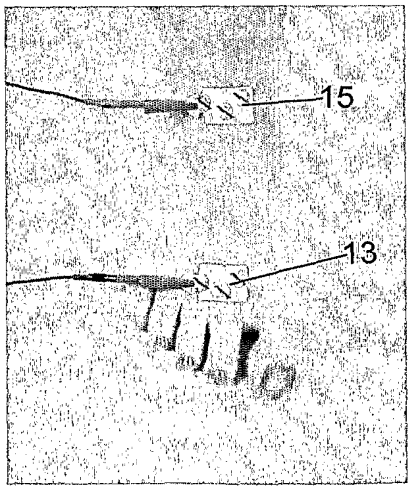

Fig. 5C

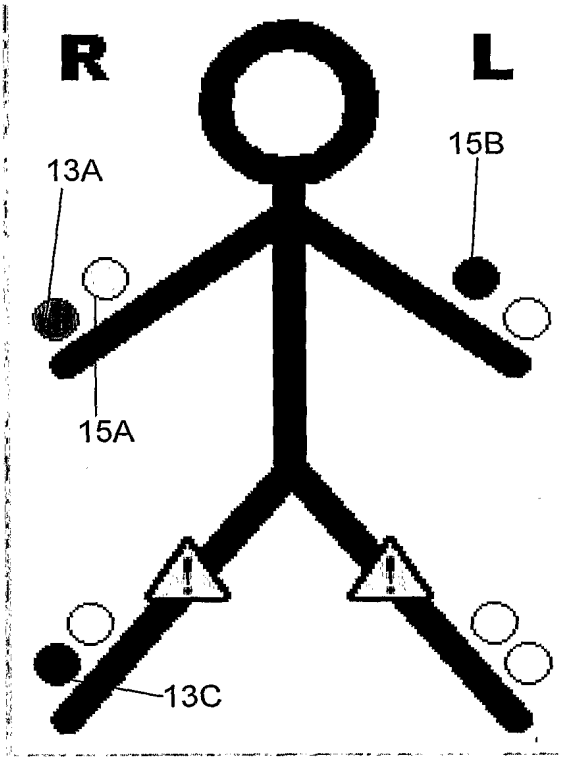
R
L
13A
15B
15A
13C

Fig. 5D

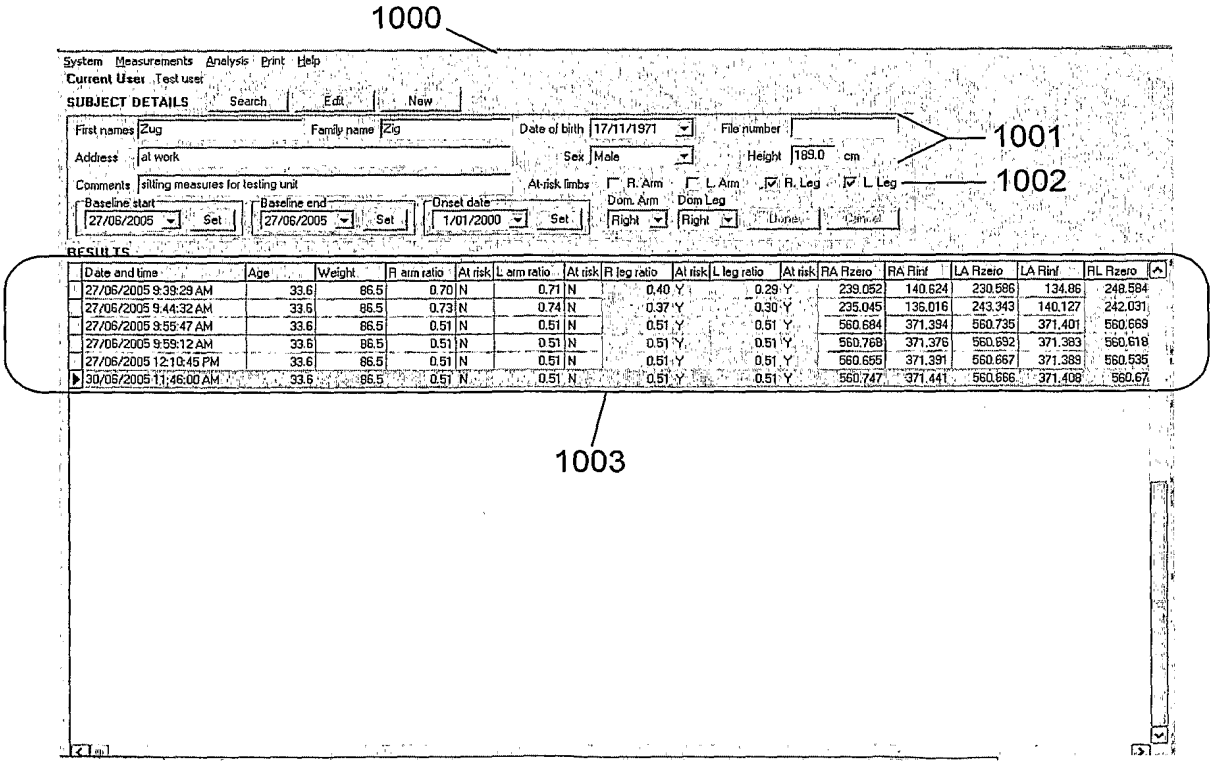
1000
System Measurements Analysis Print Help
Current User Test user
SUBJECT DETAILS
Search
Edit
New
First names Zug
Family name Zig
Date of birth 17/11/1971
File number
Address at work
Sex Male
Height 189.0 cm
Comments sitting measures for testing unit
At-risk limbs
R. Arm
L. Arm
R. Leg
L. Leg
1001
1002
Baseline start
27/06/2005
Set
Baseline end
27/06/2005
Set
Onset date
1/01/2000
Set
Dom. Arm
Right
Dom Leg
Right
Done
Cancel
RESULTS
Date and time
Age
Weight
R arm ratio
At risk
L arm ratio
At risk
R leg ratio
At risk
L leg ratio
At risk
RA Rzero
RA Rinf
LA Rzero
LA Rinf
RL Rzero
27/06/2005 9:39:29 AM 33.6 86.5 0.70 N 0.71 N 0.40 Y 0.29 Y 239.052 140.624 230.586 134.86 248.584
27/06/2005 9:44:32 AM 33.6 86.5 0.73 N 0.74 N 0.37 Y 0.30 Y 235.045 136.016 243.343 140.127 242.031
27/06/2005 9:55:47 AM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.684 371.394 560.735 371.401 560.669
27/06/2005 9:59:12 AM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.768 371.376 560.692 371.383 560.618
27/06/2005 12:10:45 PM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.655 371.391 560.667 371.389 560.535
30/06/2005 11:46:00 AM 33.6 86.5 0.51 N 0.51 N 0.51 Y 0.51 Y 560.747 371.441 560.666 371.408 560.67
1003

Fig. 5E

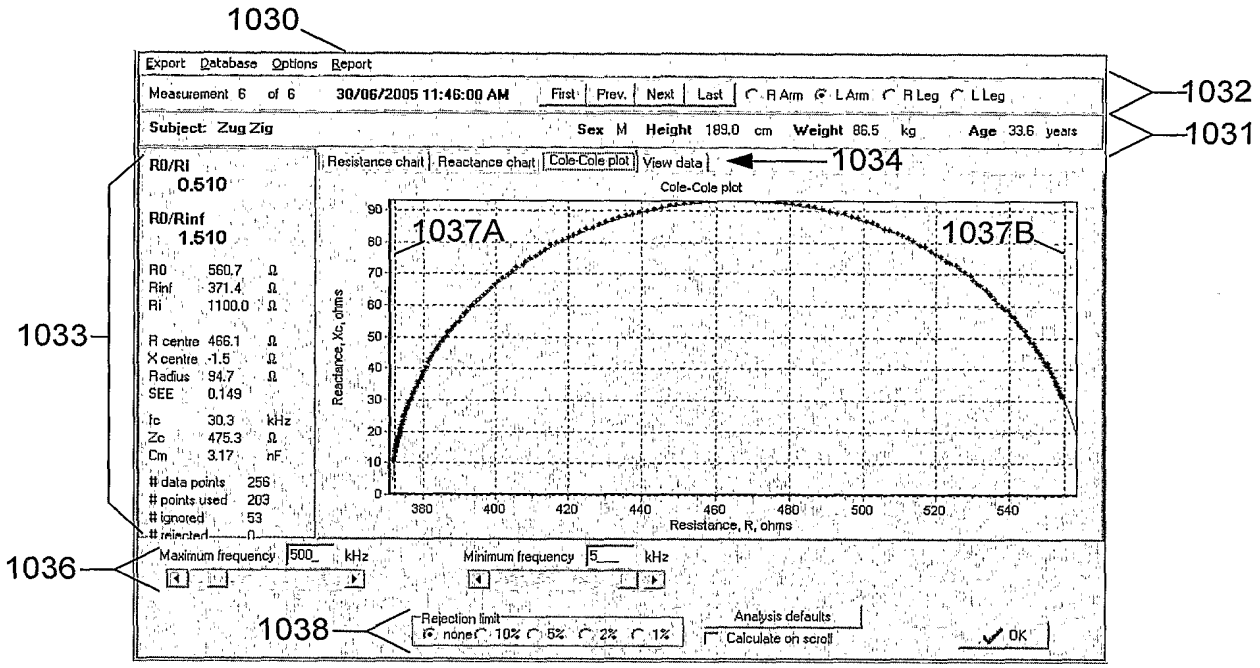
1030
Export Database Options Report
Measurement 6 of 6 30/06/2005 11:46:00 AM First Prev. Next Last R Arm L Arm R Leg L Leg
1032
Subject: Zug Zig Sex M Height 189.0 cm Weight 86.5 kg Age 33.6 years
1031
R0/Ri 0.510
R0/Rinf 1.510
R0 560.7 Ω
Rinf 371.4 Ω
Ri 1100.0 Ω
R centre 466.1 Ω
X centre -1.5 Ω
Radius 94.7 Ω
SEE 0.149
fc 30.3 kHz
Zc 475.3 Ω
Cm 3.17 nF
data points 256
points used 203
ignored 53
rejected 0
1033
Resistance chart Reactance chart Cole-Cole plot View data
1034
Cole-Cole plot
1037A
1037B
Reactance, Xc, ohms
Resistance, R, ohms
Maximum frequency 500 kHz
Minimum frequency 5 kHz
1036
Rejection limit none 10% 5% 2% 1%
Analysis defaults
Calculate on scroll
OK
1038

Fig. 6A

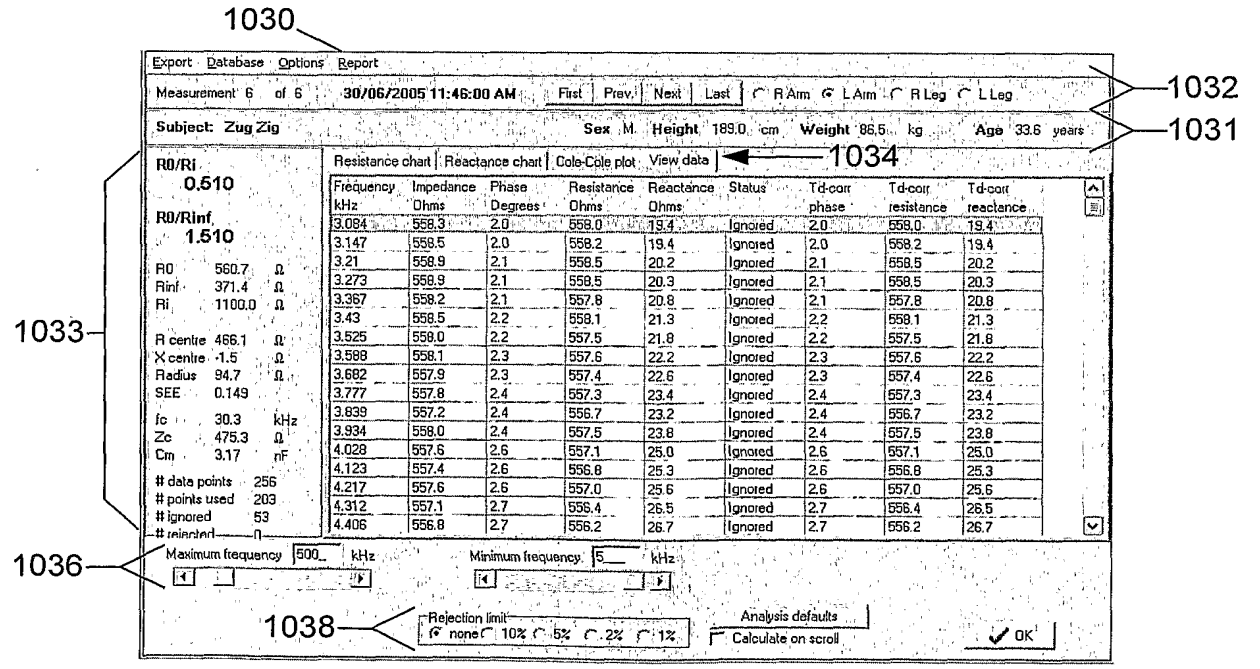
1030
Export Database Options Report
Measurement 6 of 6 30/06/2005 11:46:00 AM First Prev. Next Last R Arm L Arm R Leg L Leg
1032
Subject: Zug Zig Sex M Height 189.0 cm Weight 86.5 kg Age 33.6 years
1031
R0/Ri 0.510
R0/Rinf 1.510
R0 560.7 Ω
Rinf 371.4 Ω
Ri 1100.0 Ω
R centre 466.1 Ω
X centre -1.5 Ω
Radius 94.7 Ω
SEE 0.149
fc 30.3 kHz
Zc 475.3 Ω
Cm 3.17 nF
data points 256
points used 203
ignored 53
rejected 0
1033
Resistance chart Reactance chart Cole-Cole plot View data
1034
Frequency kHz | Impedance Ohms | Phase Degrees | Resistance Ohms | Reactance Ohms | Status | Td-corr phase | Td-corr resistance | Td-corr reactance
3.084 | 558.3 | 2.0 | 558.0 | 19.4 | Ignored | 2.0 | 558.0 | 19.4
3.147 | 558.5 | 2.0 | 558.2 | 19.4 | Ignored | 2.0 | 558.2 | 19.4
3.21 | 558.9 | 2.1 | 558.5 | 20.2 | Ignored | 2.1 | 558.5 | 20.2
3.273 | 558.9 | 2.1 | 558.5 | 20.3 | Ignored | 2.1 | 558.5 | 20.3
3.367 | 558.2 | 2.1 | 557.8 | 20.8 | Ignored | 2.1 | 557.8 | 20.8
3.43 | 558.5 | 2.2 | 558.1 | 21.3 | Ignored | 2.2 | 558.1 | 21.3
3.525 | 558.0 | 2.2 | 557.5 | 21.8 | Ignored | 2.2 | 557.5 | 21.8
3.588 | 558.1 | 2.3 | 557.6 | 22.2 | Ignored | 2.3 | 557.6 | 22.2
3.682 | 557.9 | 2.3 | 557.4 | 22.6 | Ignored | 2.3 | 557.4 | 22.6
3.777 | 557.8 | 2.4 | 557.3 | 23.4 | Ignored | 2.4 | 557.3 | 23.4
3.839 | 557.2 | 2.4 | 556.7 | 23.2 | Ignored | 2.4 | 556.7 | 23.2
3.934 | 558.0 | 2.4 | 557.5 | 23.8 | Ignored | 2.4 | 557.5 | 23.8
4.028 | 557.6 | 2.6 | 557.1 | 25.0 | Ignored | 2.6 | 557.1 | 25.0
4.123 | 557.4 | 2.6 | 556.8 | 25.3 | Ignored | 2.6 | 556.8 | 25.3
4.217 | 557.6 | 2.6 | 557.0 | 25.6 | Ignored | 2.6 | 557.0 | 25.6
4.312 | 557.1 | 2.7 | 556.4 | 26.5 | Ignored | 2.7 | 556.4 | 26.5
4.406 | 556.8 | 2.7 | 556.2 | 26.7 | Ignored | 2.7 | 556.2 | 26.7
Maximum frequency 500 kHz
Minimum frequency 5 kHz
1036
Rejection limit none 10% 5% 2% 1%
Analysis defaults
Calculate on scroll
OK
1038

Fig. 6B

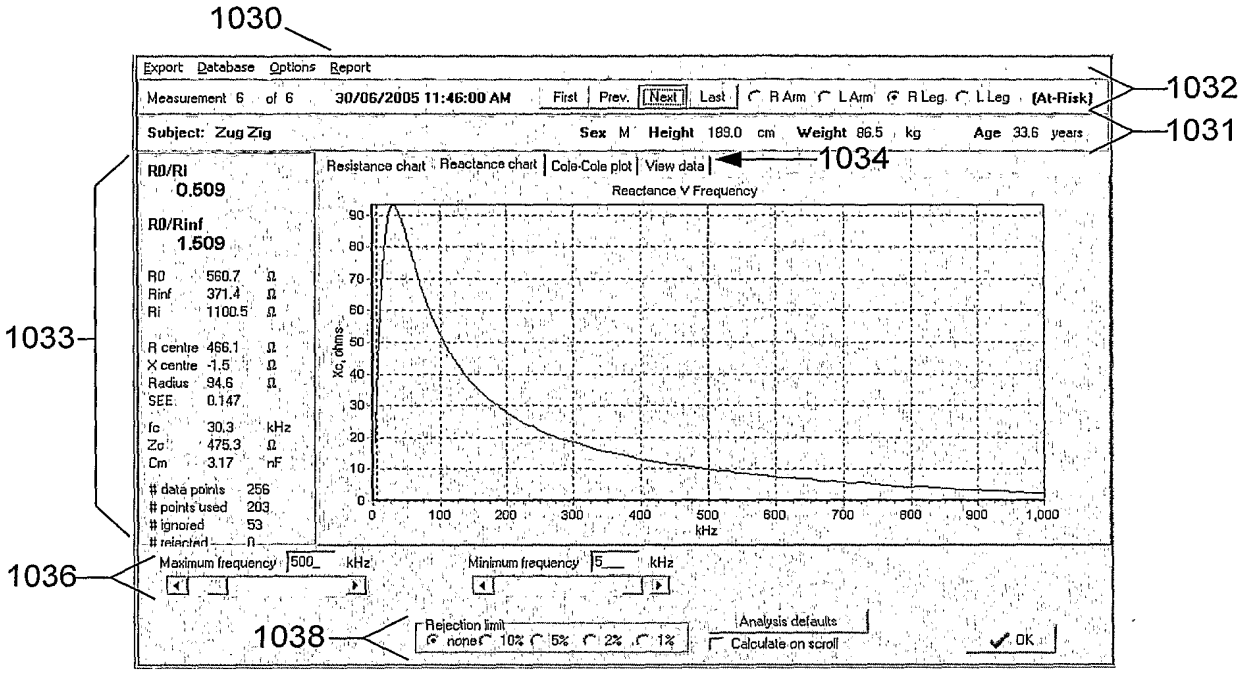
1030
Export Database Options Report
Measurement 6 of 6 30/06/2005 11:46:00 AM First Prev. Next Last R Arm L Arm R Leg L Leg (At-Risk)
1032
Subject: Zug Zig Sex M Height 189.0 cm Weight 86.5 kg Age 33.6 years
1031
R0/Ri 0.509
R0/Rinf 1.509
R0 560.7 Ω
Rinf 371.4 Ω
Ri 1100.5 Ω
R centre 466.1 Ω
X centre -1.5 Ω
Radius 94.6 Ω
SEE 0.147
fc 30.3 kHz
Zc 475.3 Ω
Cm 3.17 nF
data points 256
points used 203
ignored 53
rejected 0
1033
Resistance chart Reactance chart Cole-Cole plot View data
1034
Reactance V Frequency
Xc, ohms
kHz
1036
Maximum frequency 500 kHz
Minimum frequency 5 kHz
1038
Rejection limit none 10% 5% 2% 1%
Analysis defaults
Calculate on scroll
OK

Fig. 6C

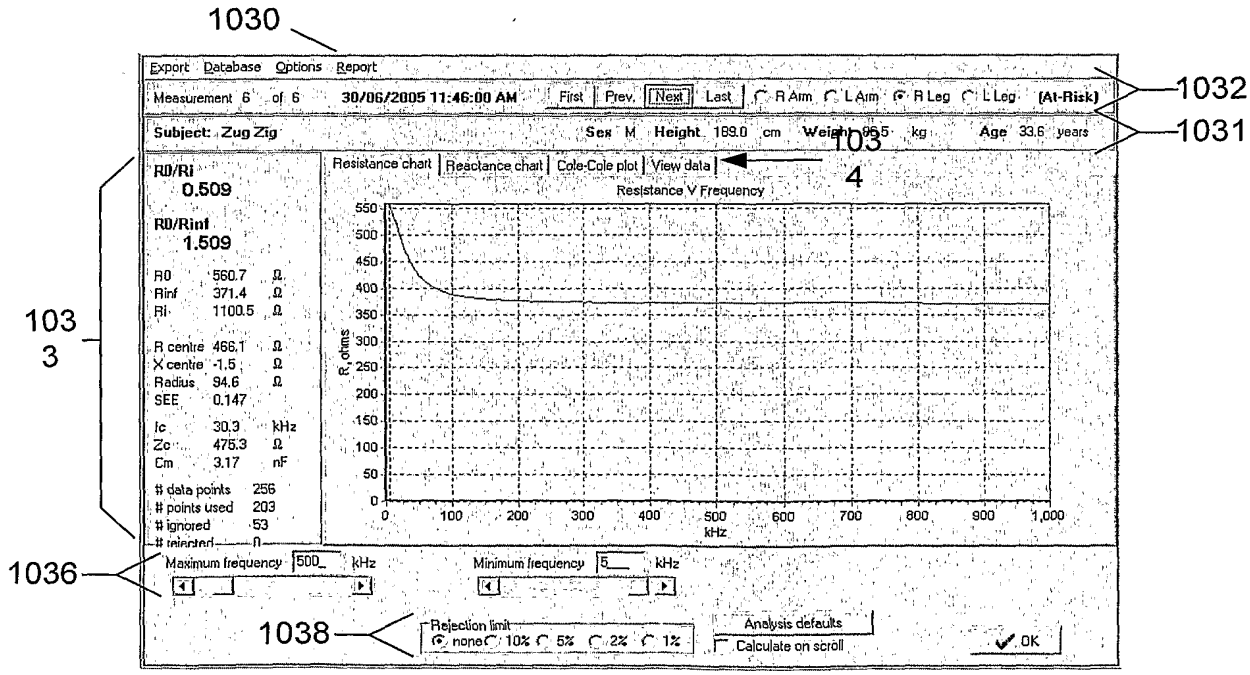
1030
Export Database Options Report
Measurement 6 of 6 30/06/2005 11:46:00 AM First Prev. Next Last R Arm L Arm R Leg L Leg (At-Risk)
1032
Subject: Zug Zig Sex M Height 189.0 cm Weight 86.5 kg Age 33.6 years
1031
R0/Ri 0.509
R0/Rinf 1.509
R0 560.7 Ω
Rinf 371.4 Ω
Ri 1100.5 Ω
R centre 466.1 Ω
X centre -1.5 Ω
Radius 94.6 Ω
SEE 0.147
fc 30.3 kHz
Zc 475.3 Ω
Cm 3.17 nF
data points 256
points used 203
ignored 53
rejected 0
103 3
Resistance chart Reactance chart Cole-Cole plot View data
103 4
Resistance V Frequency
R, ohms
kHz
1036
Maximum frequency 500 kHz
Minimum frequency 5 kHz
1038
Rejection limit none 10% 5% 2% 1%
Analysis defaults
Calculate on scroll
OK

Fig. 6D

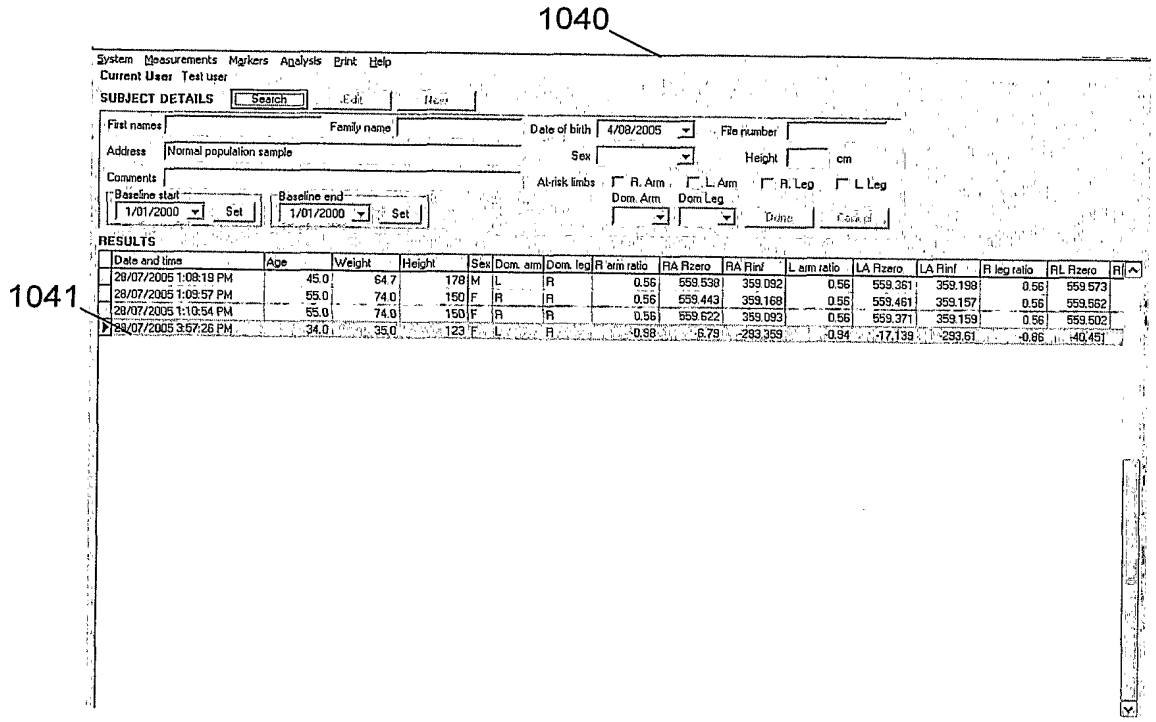
1040
1041
System Measurements Markers Analysis Print Help
Current User Test user
SUBJECT DETAILS
Search
Edit
New
First names
Family name
Date of birth 4/08/2005
File number
Address Normal population sample
Sex
Height cm
Comments
At-risk limbs R. Arm L. Arm R. Leg L. Leg
Baseline start 1/01/2000 Set
Baseline end 1/01/2000 Set
Dom. Arm
Dom Leg
Done
Cancel
RESULTS
Date and time | Age | Weight | Height | Sex | Dom. arm | Dom. leg | R arm ratio | RA Rzero | RA Rinf | L arm ratio | LA Rzero | LA Rinf | R leg ratio | RL Rzero | R
28/07/2005 1:08:19 PM | 45.0 | 64.7 | 178 | M | L | R | 0.56 | 559.538 | 359.092 | 0.56 | 559.361 | 359.198 | 0.56 | 559.573
28/07/2005 1:09:57 PM | 55.0 | 74.0 | 150 | F | R | R | 0.56 | 559.443 | 359.168 | 0.56 | 559.461 | 359.157 | 0.56 | 559.562
28/07/2005 1:10:54 PM | 55.0 | 74.0 | 150 | F | R | R | 0.56 | 559.622 | 359.093 | 0.56 | 559.371 | 359.159 | 0.56 | 559.502
28/07/2005 3:57:26 PM | 34.0 | 35.0 | 123 | F | L | R | 0.98 | 6.79 | -293.359 | 0.94 | -17.139 | 293.61 | -0.96 | -40.451

Fig. 7A

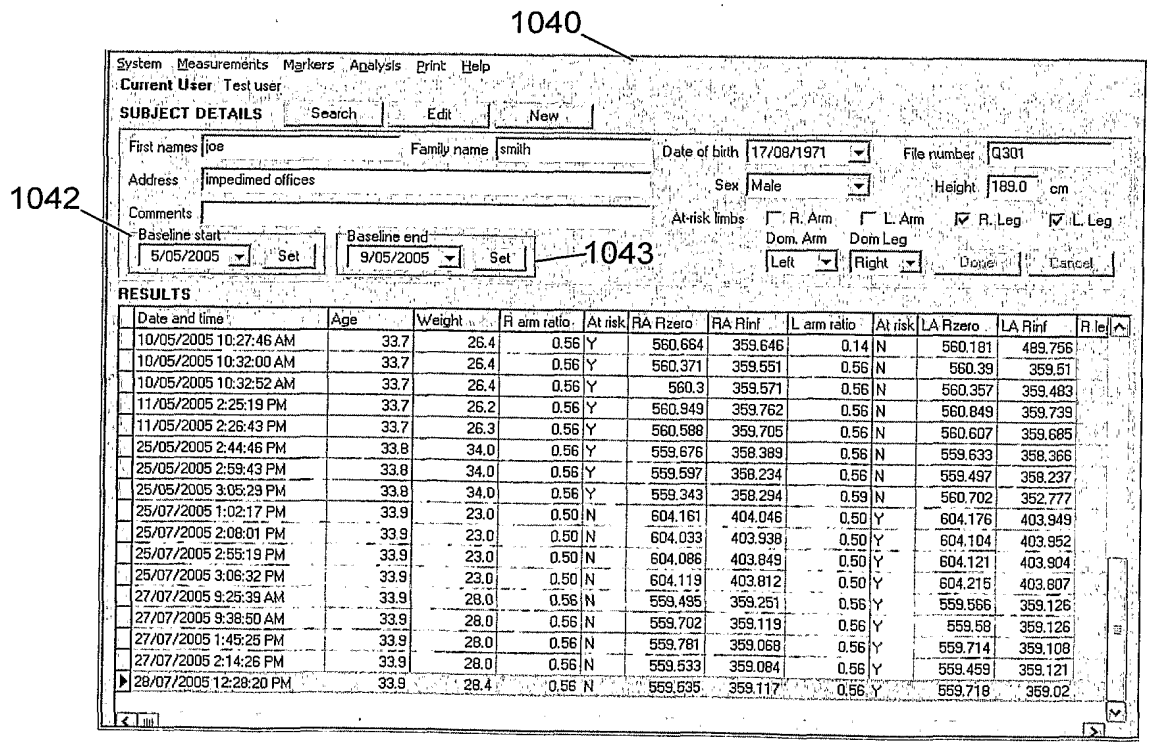
1040
1042
1043
System Measurements Markers Analysis Print Help
Current User Test user
SUBJECT DETAILS
Search
Edit
New
First names joe
Family name smith
Date of birth 17/08/1971
File number Q301
Address impedimed offices
Sex Male
Height 189.0 cm
Comments
At-risk limbs R. Arm L. Arm R. Leg L. Leg
Baseline start 5/05/2005 Set
Baseline end 9/05/2005 Set
Dom. Arm Left
Dom Leg Right
Done
Cancel
RESULTS
Date and time | Age | Weight | R arm ratio | At risk | RA Rzero | RA Rinf | L arm ratio | At risk | LA Rzero | LA Rinf | R le
10/05/2005 10:27:46 AM | 33.7 | 26.4 | 0.56 | Y | 560.664 | 359.646 | 0.14 | N | 560.181 | 489.756
10/05/2005 10:32:00 AM | 33.7 | 26.4 | 0.56 | Y | 560.371 | 359.551 | 0.56 | N | 560.39 | 359.51
10/05/2005 10:32:52 AM | 33.7 | 26.4 | 0.56 | Y | 560.3 | 359.571 | 0.56 | N | 560.357 | 359.483
11/05/2005 2:25:19 PM | 33.7 | 26.2 | 0.56 | Y | 560.949 | 359.762 | 0.56 | N | 560.849 | 359.739
11/05/2005 2:26:43 PM | 33.7 | 26.3 | 0.56 | Y | 560.588 | 359.705 | 0.56 | N | 560.607 | 359.685
25/05/2005 2:44:46 PM | 33.8 | 34.0 | 0.56 | Y | 559.676 | 358.389 | 0.56 | N | 559.633 | 358.366
25/05/2005 2:59:43 PM | 33.8 | 34.0 | 0.56 | Y | 559.597 | 358.234 | 0.56 | N | 559.497 | 358.237
25/05/2005 3:05:29 PM | 33.8 | 34.0 | 0.56 | Y | 559.343 | 358.294 | 0.59 | N | 560.702 | 352.777
25/07/2005 1:02:17 PM | 33.9 | 23.0 | 0.50 | N | 604.161 | 404.046 | 0.50 | Y | 604.176 | 403.949
25/07/2005 2:08:01 PM | 33.9 | 23.0 | 0.50 | N | 604.033 | 403.938 | 0.50 | Y | 604.104 | 403.952
25/07/2005 2:55:19 PM | 33.9 | 23.0 | 0.50 | N | 604.086 | 403.849 | 0.50 | Y | 604.121 | 403.904
25/07/2005 3:06:32 PM | 33.9 | 23.0 | 0.50 | N | 604.119 | 403.812 | 0.50 | Y | 604.215 | 403.807
27/07/2005 9:25:39 AM | 33.9 | 28.0 | 0.56 | N | 559.495 | 359.251 | 0.56 | Y | 559.566 | 359.126
27/07/2005 9:38:50 AM | 33.9 | 28.0 | 0.56 | N | 559.702 | 359.119 | 0.56 | Y | 559.58 | 359.126
27/07/2005 1:45:25 PM | 33.9 | 28.0 | 0.56 | N | 559.781 | 359.068 | 0.56 | Y | 559.714 | 359.108
27/07/2005 2:14:26 PM | 33.9 | 28.0 | 0.56 | N | 559.533 | 359.084 | 0.56 | Y | 559.459 | 359.121
28/07/2005 12:28:20 PM | 33.9 | 28.4 | 0.56 | N | 559.535 | 359.117 | 0.56 | Y | 559.718 | 359.02

Fig. 7B

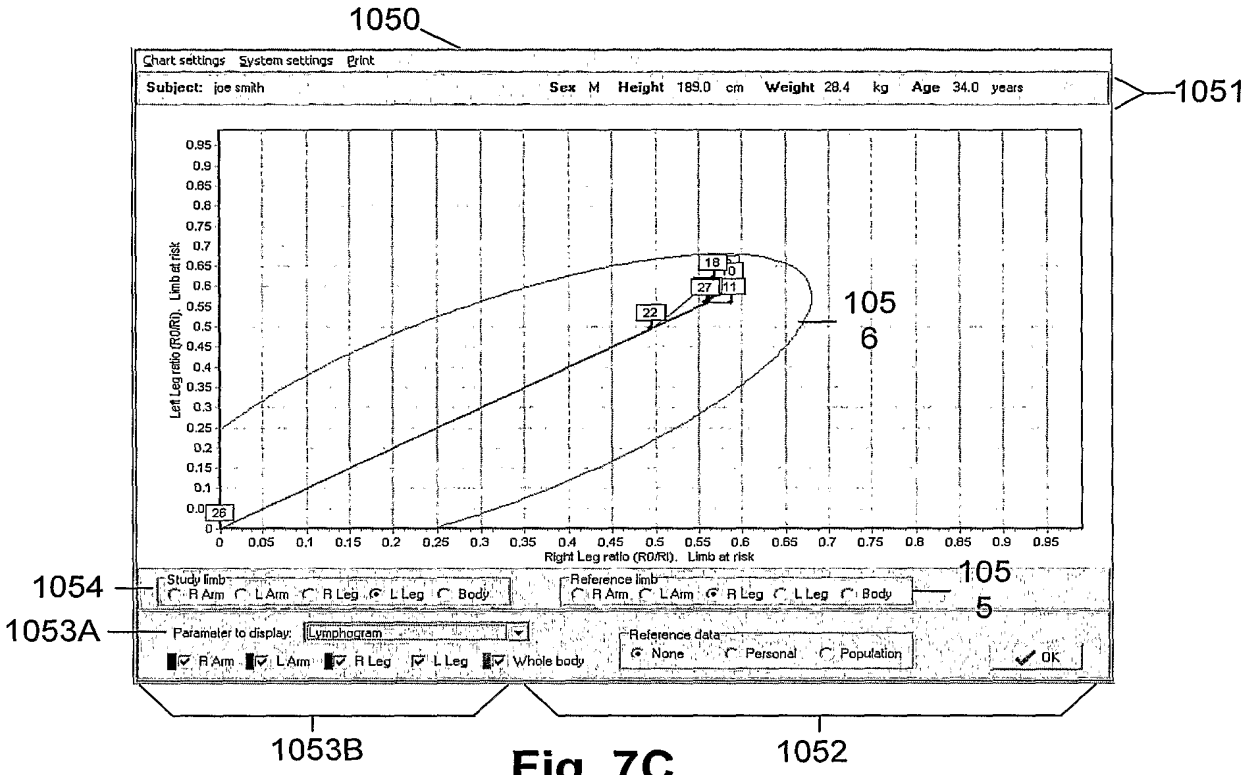
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
Left Leg ratio (R0/R0). Limb at risk
Right Leg ratio (R0/R0). Limb at risk
1056
1054
1055
1053A
Study limb
R Arm L Arm R Leg L Leg Body
Reference limb
R Arm L Arm R Leg L Leg Body
Parameter to display: Lymphogram
R Arm L Arm R Leg L Leg Whole body
Reference data
None Personal Population
OK
1053B
1052

Fig. 7C

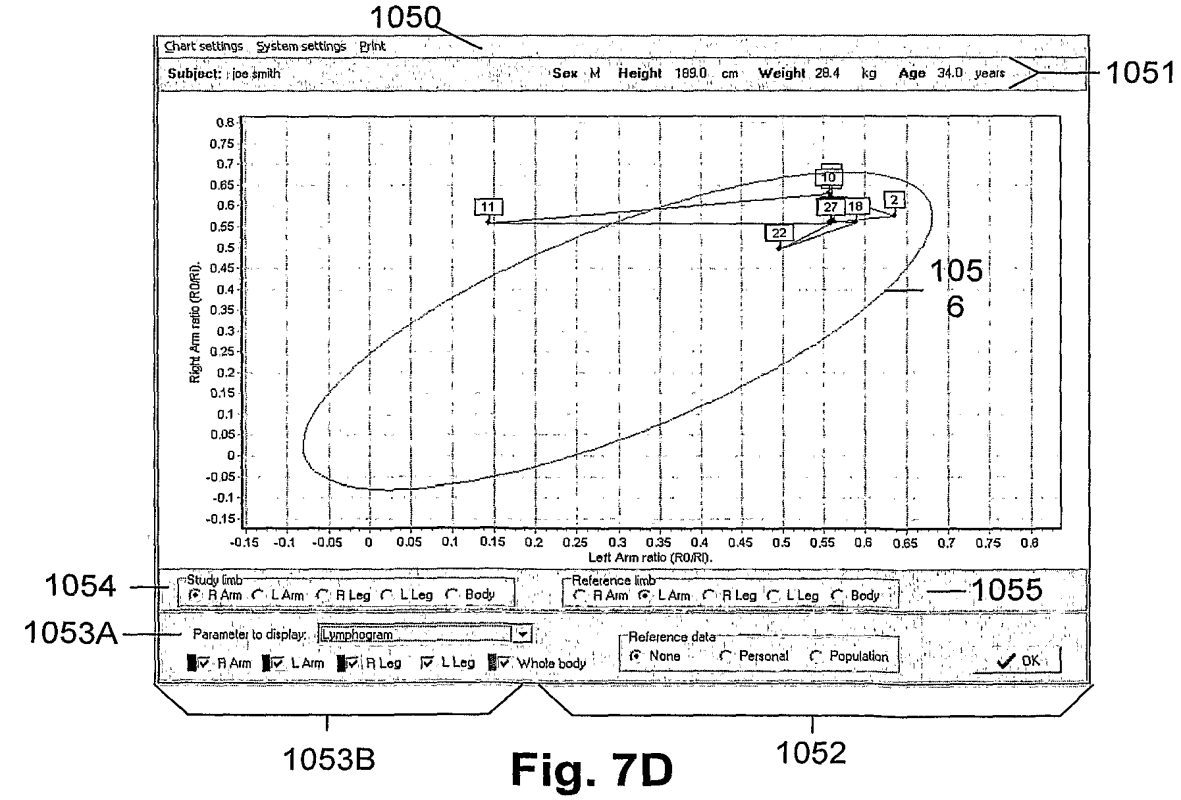
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
Right Arm ratio (R0/R0).
Left Arm ratio (R0/R0).
1056
1054
1055
1053A
Study limb
R Arm L Arm R Leg L Leg Body
Reference limb
R Arm L Arm R Leg L Leg Body
Parameter to display: Lymphogram
R Arm L Arm R Leg L Leg Whole body
Reference data
None Personal Population
OK
1053B
1052

Fig. 7D

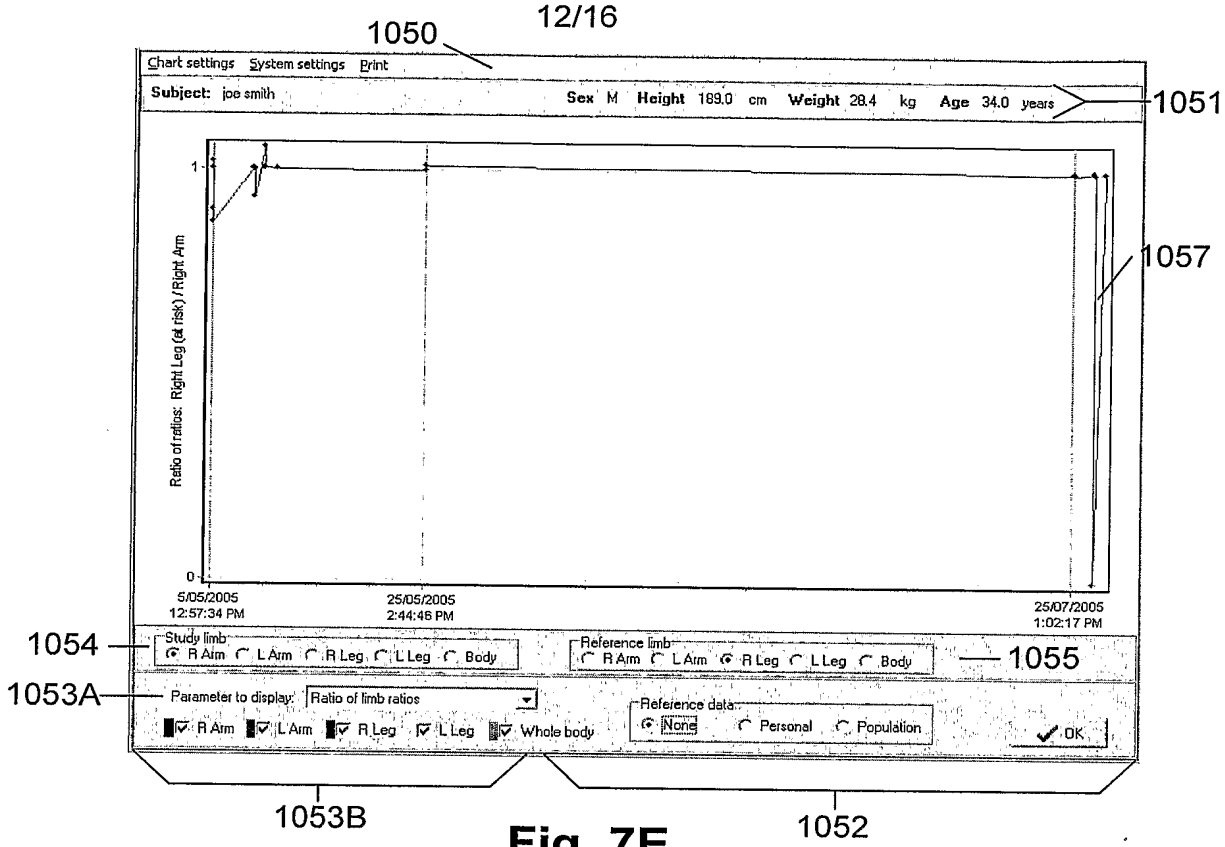
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
1057
Ratio of ratios: Right Leg (at risk) / Right Arm
1
0
5/05/2005 12:57:34 PM
25/05/2005 2:44:46 PM
25/07/2005 1:02:17 PM
1054
Study limb
R Arm L Arm R Leg L Leg Body
Reference limb
R Arm L Arm R Leg L Leg Body
1055
1053A
Parameter to display: Ratio of limb ratios
R Arm L Arm R Leg L Leg Whole body
Reference data:
None Personal Population
OK
1053B
1052

Fig. 7E

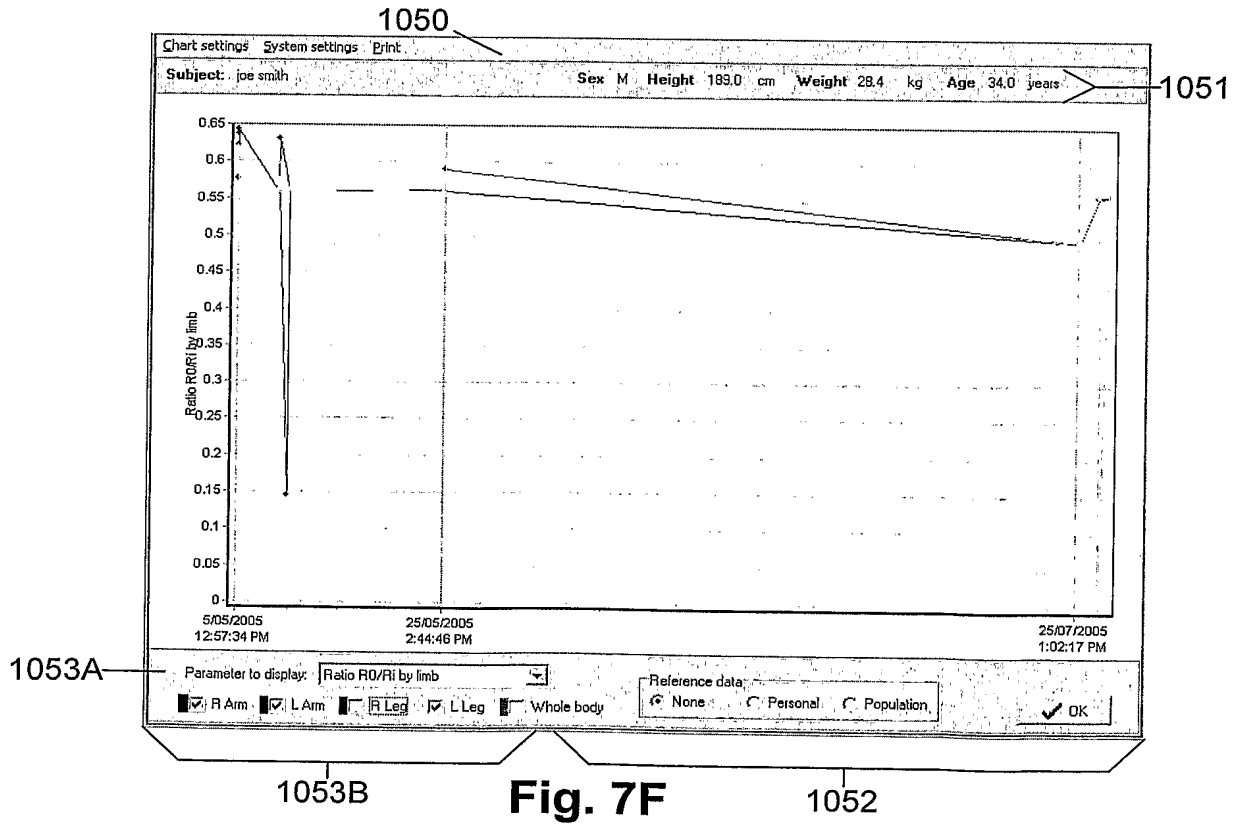
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
0.65
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Ratio RO/Ri by limb
5/05/2005 12:57:34 PM
25/05/2005 2:44:46 PM
25/07/2005 1:02:17 PM
1053A
Parameter to display: Ratio RO/Ri by limb
R Arm L Arm R Leg L Leg Whole body
Reference data:
None Personal Population
OK
1053B
1052

Fig. 7F

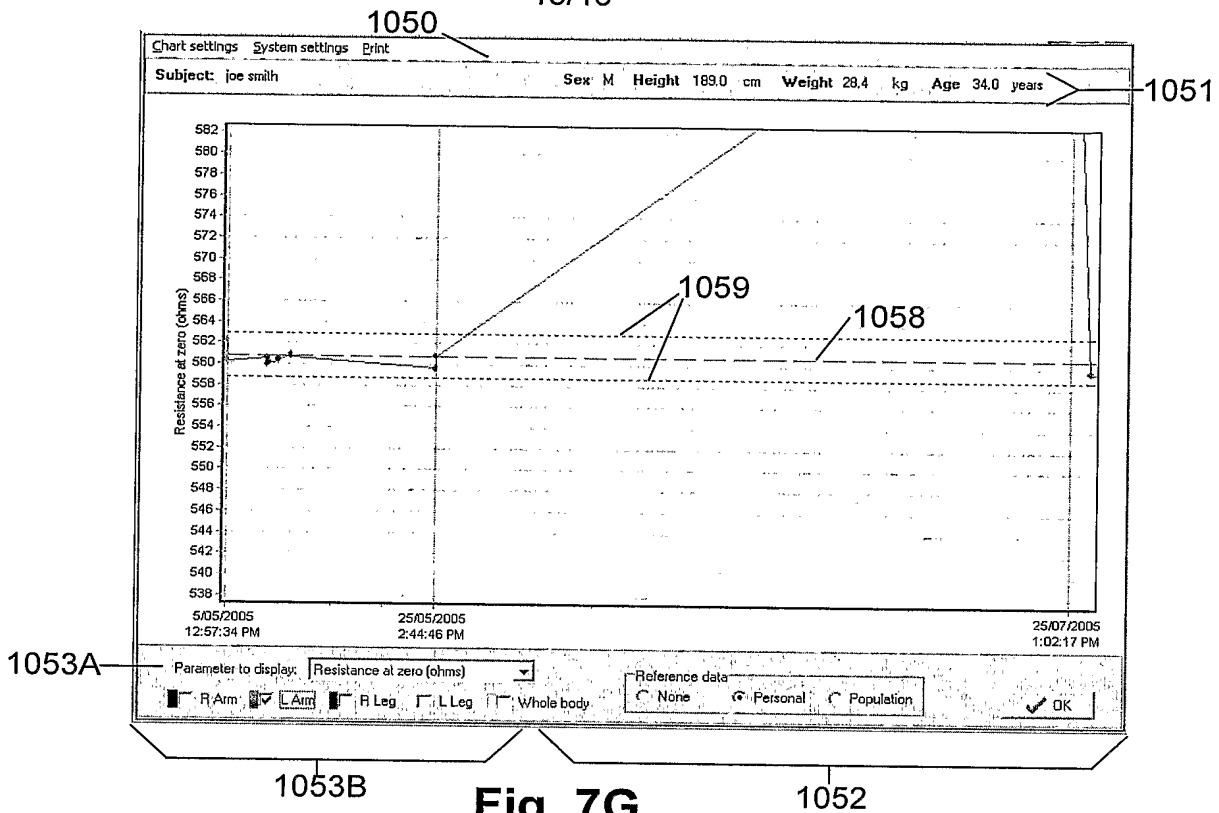
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
Resistance at zero (ohms)
582
580
578
576
574
572
570
568
566
564
562
560
558
556
554
552
550
548
546
544
542
540
538
1059
1058
5/05/2005 12:57:34 PM
25/05/2005 2:44:46 PM
25/07/2005 1:02:17 PM
1053A
Parameter to display: Resistance at zero (ohms)
R Arm L Arm R Leg L Leg Whole body
Reference data
None Personal Population
OK
1053B
1052

Fig. 7G

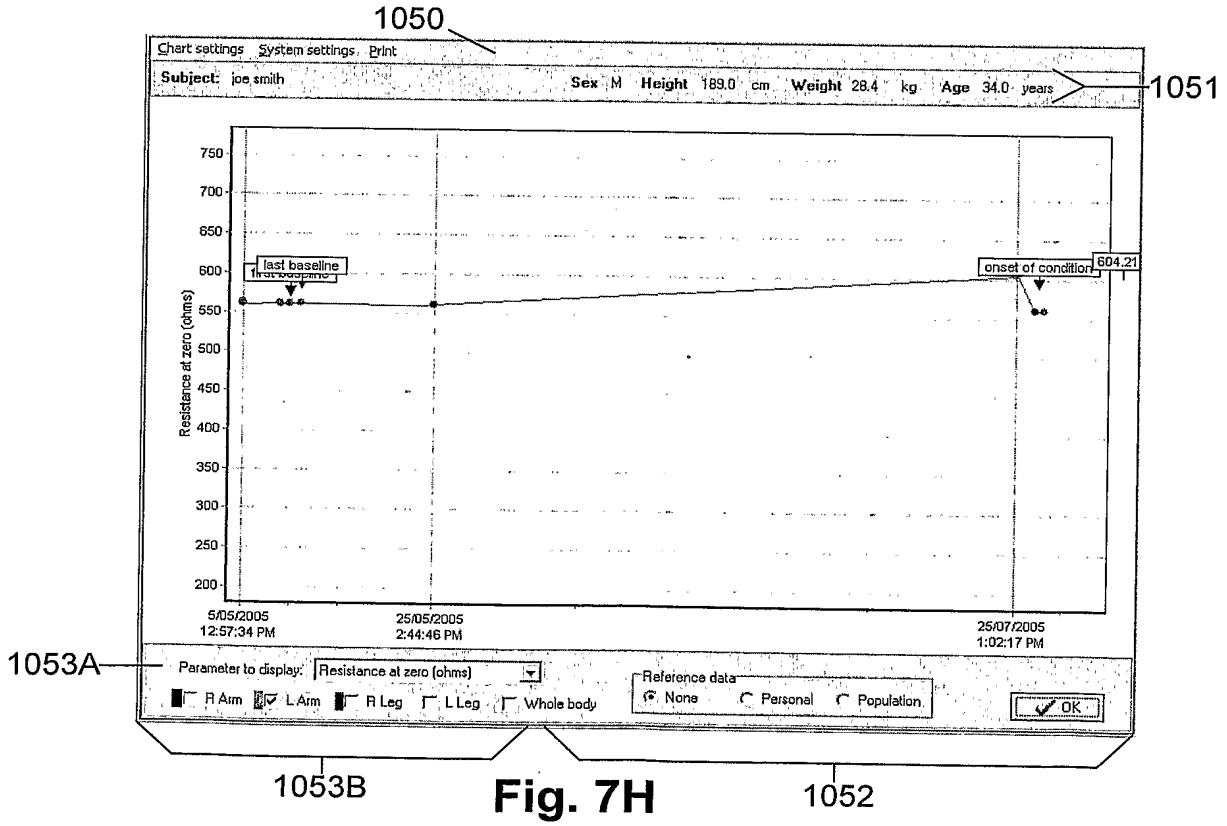
1050
Chart settings System settings Print
Subject: joe smith
Sex M Height 189.0 cm Weight 28.4 kg Age 34.0 years
1051
Resistance at zero (ohms)
750
700
650
600
550
500
450
400
350
300
250
200
last baseline
onset of condition
604.21
5/05/2005 12:57:34 PM
25/05/2005 2:44:46 PM
25/07/2005 1:02:17 PM
1053A
Parameter to display: Resistance at zero (ohms)
R Arm L Arm R Leg L Leg Whole body
Reference data
None Personal Population
OK
1053B
1052

Fig. 7H

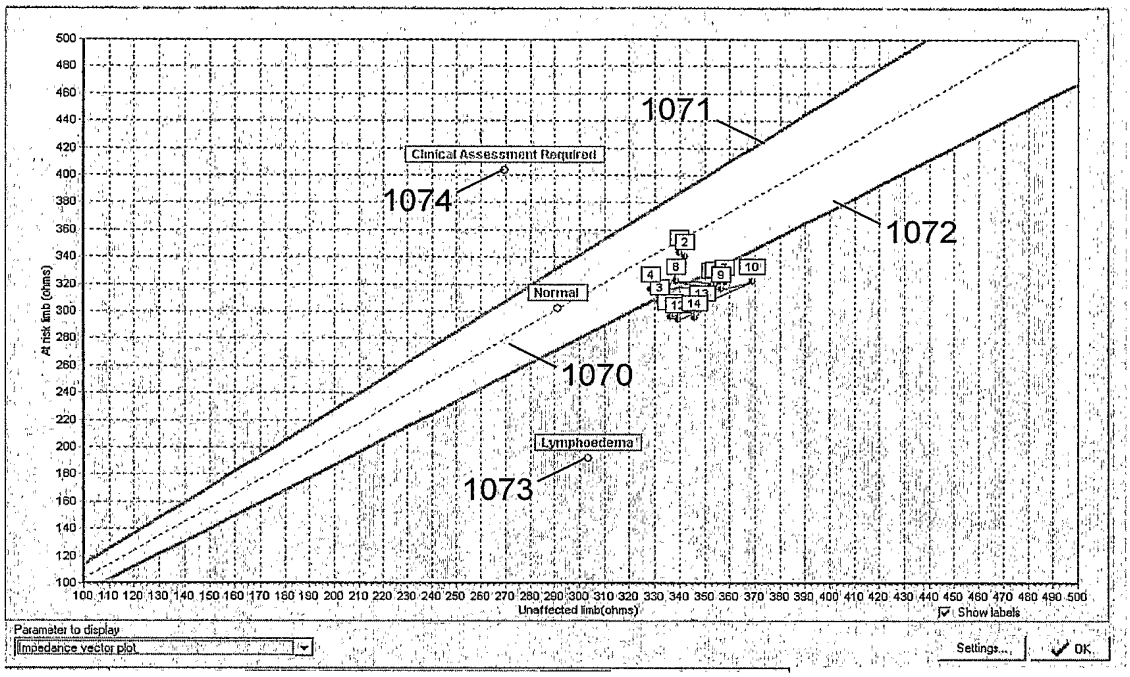
1071
Clinical Assessment Required
1074
1072
Normal
1070
Lymphoedema
1073
At risk limb (ohms)
Unaffected limb(ohms)
Show labels
Parameter to display
Impedance vector plot
Settings...
OK

Fig. 7I

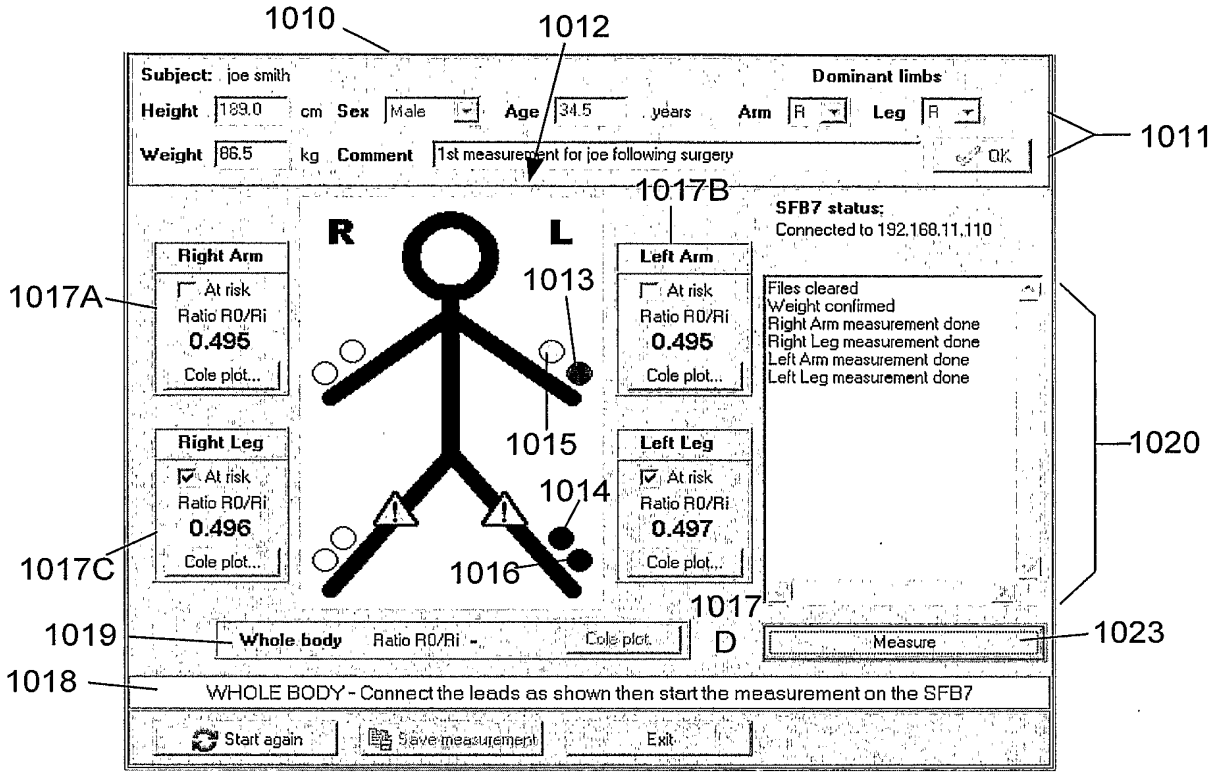
1010
1012
1011
1017B
1017A
1013
1015
1014
1016
1017C
1017
D
1019
1018
1020
1023
Subject: joe smith
Dominant limbs
Height 189.0 cm Sex Male Age 34.5 years Arm R Leg R
Weight 86.5 kg Comment 1st measurement for joe following surgery
OK
SFB7 status:
Connected to 192.168.11.110
R
L
Right Arm
At risk
Ratio R0/Ri
0.495
Cole plot...
Left Arm
At risk
Ratio R0/Ri
0.495
Cole plot...
Right Leg
At risk
Ratio R0/Ri
0.496
Cole plot...
Left Leg
At risk
Ratio R0/Ri
0.497
Cole plot...
Files cleared
Weight confirmed
Right Arm measurement done
Right Leg measurement done
Left Arm measurement done
Left Leg measurement done
Whole body Ratio R0/Ri - Cole plot
Measure
WHOLE BODY - Connect the leads as shown then start the measurement on the SFB7
Start again
Save measurement
Exit

Fig. 8

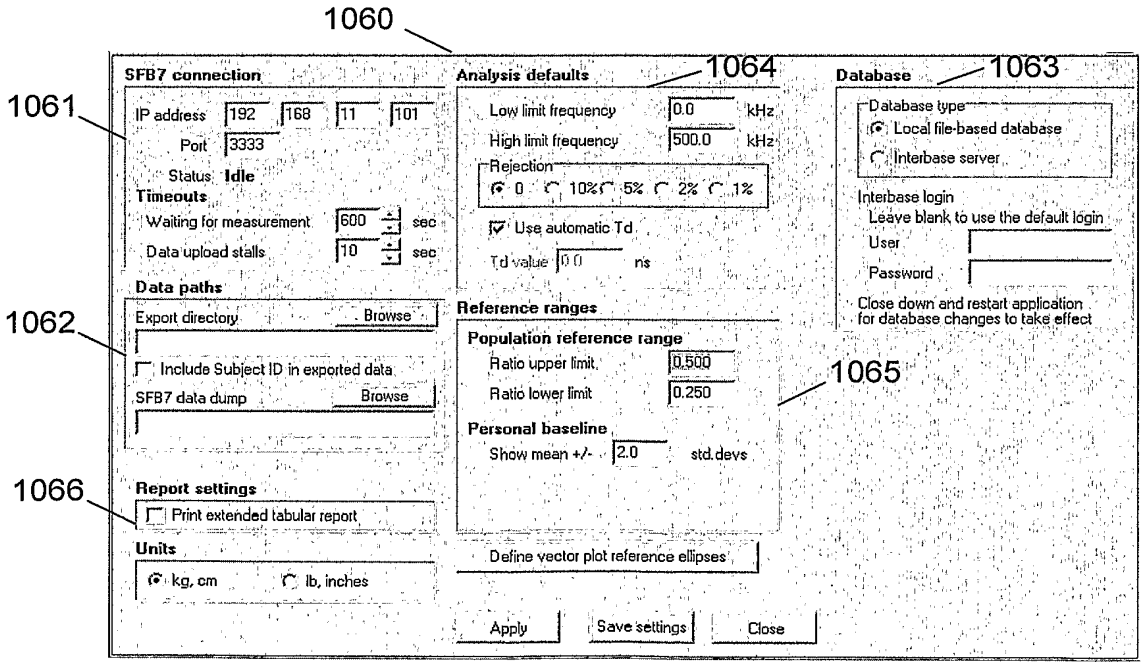
1060
1061
1062
1066
1064
1063
1065
SFB7 connection
IP address 192 168 11 101
Port 3333
Status Idle
Timeouts
Waiting for measurement 600 sec
Data upload stalls 10 sec
Data paths
Export directory Browse
Include Subject ID in exported data
SFB7 data dump Browse
Report settings
Print extended tabular report
Units
kg, cm lb, inches
Analysis defaults
Low limit frequency 0.0 kHz
High limit frequency 500.0 kHz
Rejection
0 10% 5% 2% 1%
Use automatic Td
Td value 0.0 ns
Reference ranges
Population reference range
Ratio upper limit 0.500
Ratio lower limit 0.250
Personal baseline
Show mean +/- 2.0 std.devs
Define vector plot reference ellipses
Database
Database type
Local file-based database
Interbase server
Interbase login
Leave blank to use the default login
User
Password
Close down and restart application for database changes to take effect
Apply
Save settings
Close

Fig. 10

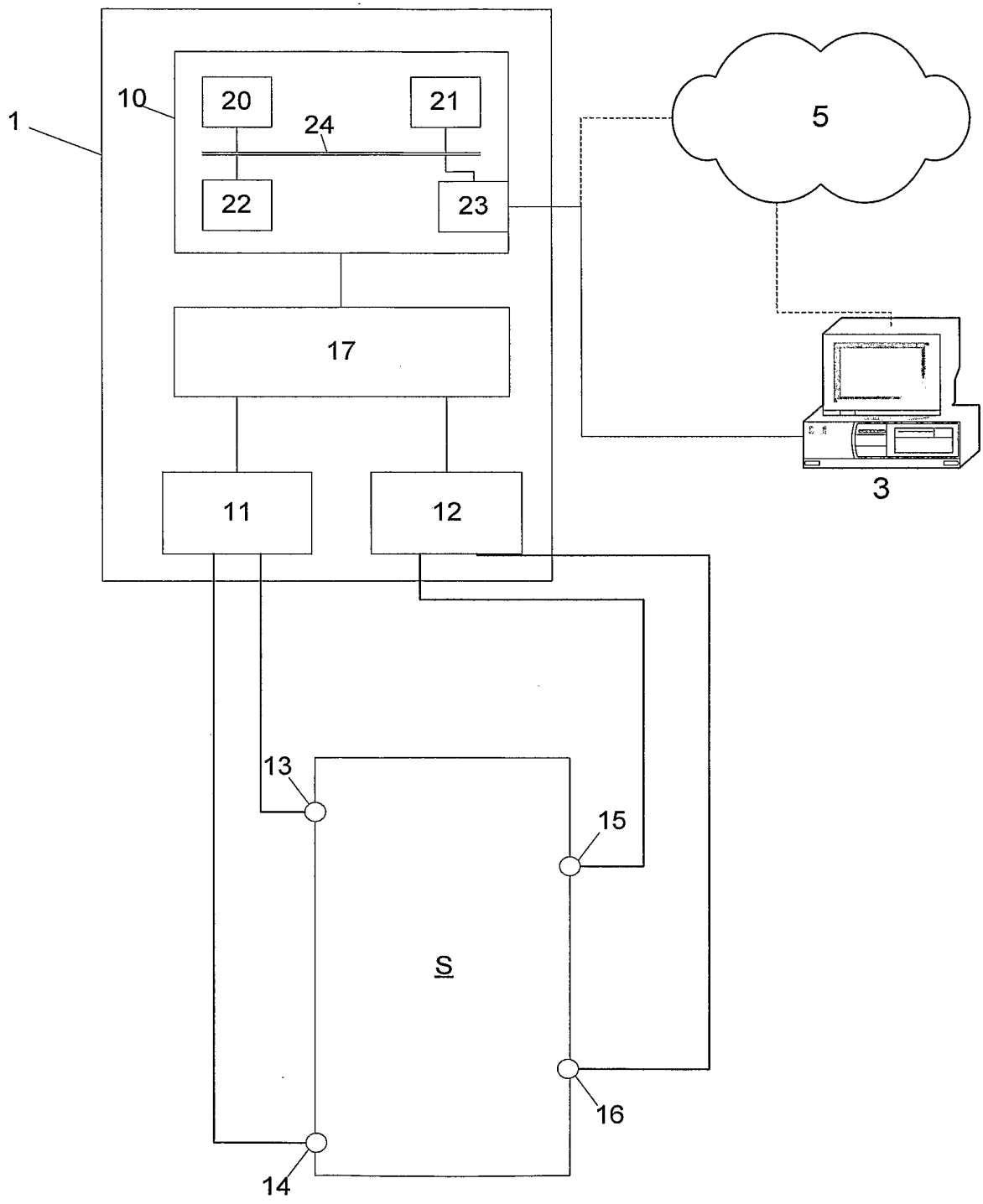

Fig. 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2006/001491

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

A61B 5/053 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DWPI and IPC Mark A61B and keywords: hydration and impedance and dialysis and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2005/122888 A1 (UNIVERSITY OF QUEENSLAND et al.) 29 December 2005 Whole document	1-11,14-17, 21-36
X	US 6151523 A (ROSELL FERRER et al.) 21 November 2000 Column 5 lines 12 to 43, column 7 line 66 to column 8 line 1	1-11,14-18, 21-36
Y		19,20,37
X	US 6496725 B2 (KAMADA et al.) 17 December 2002 Column 7 line 50 to column 8 line 13	1-11,14-17, 21-36
Y		18-20,37
X	US 6643543 B2 (TAKEHARA et al.) 4 November 2003 Column 2 lines 44 to 67	1-11,14-17, 21-36
Y		18-20,37

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 November 2006	24 NOV 2006
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer **DAVID MELHUISH** Telephone No : (02) 6283 2426

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2005/018432 A2 (PHILOMETRON, INC.) 3 March 2005 Page 11 paragraph 2 Page 26 line 28 to page 27 line 8, page 34 lines 12 to 20	18-20,37
X Y	US 2003/0120170 A1 (ZHU et al.) 26 June 2003 Paragraphs 7 and 84	1-17,21-37 18-20
X Y	US 2005/0039763 A1 (KRAEMER et al.) 24 February 2005 Paragraphs 9 and 10	1-11,14-17, 21-37 18-20
A	US 2004/0167423 A1 (PILLON et al.) 26 August 2004 Whole document	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU2006/001491

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	2005122888	NIL					
US	6151523	EP	0865763	ES	2151774		
US	6496725	CN	1308920	EP	1112715	JP	2001187035
		US	2001007924				
US	6643543	EP	1177760	JP	2002045346	US	2002022787
WO	2005018432	AU	2004266725	CA	2539547	EP	1677674
		US	2005070778				
US	2003120170	AU	84863/01	AU	2003293091	CA	2418974
		EP	1309273	EP	1645227	US	6615077
		US	2006122540	WO	0213691	WO	2004049938
		WO	2006042218				
US	2005039763	AU	2002235772	EP	1455646	US	7133716
		WO	03053239				
US	2004167423	NIL					

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX